SEQUENCE LISTING

<110> Flynn, Daniel L.
Kaufman, Michael D.

<120> PYRIDONE AMIDES AND ANALOGS EXHIBITING ANTI-CANCER AND ANTI-PROLIFERATIVE ACTIVITIES

<130> DECP-051/01US 313114-2291

<150> US 61/562,602
<151> 2011-11-22

<160> 4

<170> PatentIn version 3.5

<210> 1
<211> 676
<212> PRT
<213> Artificial Sequence

<220>
<223> c-KIT with N-terminal CST fusion

<400> 1

Leu Gly Tyr Trp Lys Ile Lys Gly Leu Val Gln Pro Thr Arg Leu Leu
1 5 10 15

Leu Glu Tyr Leu Glu Glu Lys Tyr Glu Glu His Leu Tyr Glu Arg Asp
20 25 30

Glu Gly Asp Lys Trp Arg Asn Lys Lys Phe Glu Leu Gly Leu Glu Phe
35 40 45

Pro Asn Leu Pro Tyr Tyr Ile Asp Gly Asp Val Lys Leu Thr Gln Ser
50 55 60

Met Ala Ile Ile Arg Tyr Ile Ala Asp Lys His Asn Met Leu Gly Gly
65 70 75 80

Cys Pro Lys Glu Arg Ala Glu Ile Ser Met Leu Glu Gly Ala Val Asp
85 90 95

Ile Arg Tyr Gly Val Ser Arg Ile Ala Tyr Ser Lys Asp Phe Glu Thr
100 105 110

Leu Lys Val Asp Phe Leu Ser Lys Leu Pro Glu Met Leu Lys Met Phe
115 120 125

Glu Asp Arg Leu Cys His Lys Thr Tyr Leu Asn Gly Asp His Val Thr
130 135 140

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His Pro Asp Phe Met Leu Tyr Asp Ala Leu Asp Val Val Leu Tyr Met
145                 150                 155                 160

Asp Pro Met Cys Leu Asp Ala Phe Pro Lys Leu Val Cys Phe Lys Lys
                165                 170                 175

Arg Ile Glu Ala Ile Pro Gln Ile Asp Lys Tyr Leu Lys Ser Ser Lys
            180                 185                 190

Tyr Ile Trp Pro Leu Gln Gly Trp Gln Ala Thr Phe Gly Gly Gly Asp
        195                 200                 205

His Pro Pro Lys Ser Asp Leu Val Pro Arg His Asn Gln Thr Ser Leu
    210                 215                 220

Tyr Lys Lys Ala Gly Ser Ala Ala Ala Val Leu Glu Glu Asn Leu Tyr
225                 230                 235                 240

Phe Gln Gly Thr Tyr Lys Tyr Leu Gln Lys Pro Met Tyr Glu Val Gln
                245                 250                 255

Trp Lys Val Val Glu Glu Ile Asn Gly Asn Asn Tyr Val Tyr Ile Asp
            260                 265                 270

Pro Thr Gln Leu Pro Tyr Asp His Lys Trp Glu Phe Pro Arg Asn Arg
        275                 280                 285

Leu Ser Phe Gly Lys Thr Leu Gly Ala Gly Ala Phe Gly Lys Val Val
    290                 295                 300

Glu Ala Thr Ala Tyr Gly Leu Ile Lys Ser Asp Ala Ala Met Thr Val
305                 310                 315                 320

Ala Val Lys Met Leu Lys Pro Ser Ala His Leu Thr Glu Arg Glu Ala
                325                 330                 335

Leu Met Ser Glu Leu Lys Val Leu Ser Tyr Leu Gly Asn His Met Asn
            340                 345                 350

Ile Val Asn Leu Leu Gly Ala Cys Thr Ile Gly Gly Pro Thr Leu Val
        355                 360                 365

Ile Thr Glu Tyr Cys Cys Tyr Gly Asp Leu Leu Asn Phe Leu Arg Arg
    370                 375                 380

Lys Arg Asp Ser Phe Ile Cys Ser Lys Gln Glu Asp His Ala Glu Ala
385                 390                 395                 400
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```
Ala Leu Tyr Lys Asn Leu Leu His Ser Lys Glu Ser Ser Cys Ser Asp
                405                 410                 415

Ser Thr Asn Glu Tyr Met Asp Met Lys Pro Gly Val Ser Tyr Val Val
            420                 425                 430

Pro Thr Lys Ala Asp Lys Arg Arg Ser Val Arg Ile Gly Ser Tyr Ile
        435                 440                 445

Glu Arg Asp Val Thr Pro Ala Ile Met Glu Asp Asp Glu Leu Ala Leu
    450                 455                 460

Asp Leu Glu Asp Leu Leu Ser Phe Ser Tyr Gln Val Ala Lys Gly Met
465                 470                 475                 480

Ala Phe Leu Ala Ser Lys Asn Cys Ile His Arg Asp Leu Ala Ala Arg
                485                 490                 495

Asn Ile Leu Leu Thr His Gly Arg Ile Thr Lys Ile Cys Asp Phe Gly
            500                 505                 510

Leu Ala Arg Asp Ile Lys Asn Asp Ser Asn Tyr Val Val Lys Gly Asn
        515                 520                 525

Ala Arg Leu Pro Val Lys Trp Met Ala Pro Glu Ser Ile Phe Asn Cys
    530                 535                 540

Val Tyr Thr Phe Glu Ser Asp Val Trp Ser Tyr Gly Ile Phe Leu Trp
545                 550                 555                 560

Glu Leu Phe Ser Leu Gly Ser Ser Pro Tyr Pro Gly Met Pro Val Asp
                565                 570                 575

Ser Lys Phe Tyr Lys Met Ile Lys Glu Gly Phe Arg Met Leu Ser Pro
            580                 585                 590

Glu His Ala Pro Ala Glu Met Tyr Asp Ile Met Lys Thr Cys Trp Asp
        595                 600                 605

Ala Asp Pro Leu Lys Arg Pro Thr Phe Lys Gln Ile Val Gln Leu Ile
    610                 615                 620

Glu Lys Gln Ile Ser Glu Ser Thr Asn His Ile Tyr Ser Asn Leu Ala
625                 630                 635                 640

Asn Cys Ser Pro Asn Arg Gln Lys Pro Val Val Asp His Ser Val Arg
                645                 650                 655
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Ile Asn Ser Val Gly Ser Thr Ala Ser Ser Ser Gln Pro Leu Leu Val
            660                 665                 670

His Asp Asp Val
        675


<210>  2
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<212>  PRT
<213>  Unknown

<220>
<223>  c-MET kinase

<400>  2

Met Ser Tyr Tyr His His His His His His Asp Tyr Asp Ile Pro Thr
1               5                   10                  15

Thr Glu Asn Leu Tyr Phe Gln Gly Ala Met Leu Val Pro Arg Gly Ser
            20                  25                  30

Pro Trp Ile Pro Phe Thr Met Lys Lys Arg Lys Gln Ile Lys Asp Leu
        35                  40                  45

Gly Ser Glu Leu Val Arg Tyr Asp Ala Arg Val His Thr Pro His Leu
    50                  55                  60

Asp Arg Leu Val Ser Ala Arg Ser Val Ser Pro Thr Thr Glu Met Val
65                  70                  75                  80

Ser Asn Glu Ser Val Asp Tyr Arg Ala Thr Phe Pro Glu Asp Gln Phe
                85                  90                  95

Pro Asn Ser Ser Gln Asn Gly Ser Cys Arg Gln Val Gln Tyr Pro Leu
            100                 105                 110

Thr Asp Met Ser Pro Ile Leu Thr Ser Gly Asp Ser Asp Ile Ser Ser
        115                 120                 125

Pro Leu Leu Gln Asn Thr Val His Ile Asp Leu Ser Ala Leu Asn Pro
    130                 135                 140

Glu Leu Val Gln Ala Val Gln His Val Val Ile Gly Pro Ser Ser Leu
145                 150                 155                 160

Ile Val His Phe Asn Glu Val Ile Gly Arg Gly His Phe Gly Cys Val
                165                 170                 175
```

```
Tyr His Gly Thr Leu Leu Asp Asn Asp Gly Lys Lys Ile His Cys Ala
            180                 185                 190

Val Lys Ser Leu Asn Arg Ile Thr Asp Ile Gly Glu Val Ser Gln Phe
        195                 200                 205

Leu Thr Glu Gly Ile Ile Met Lys Asp Phe Ser His Pro Asn Val Leu
    210                 215                 220

Ser Leu Leu Gly Ile Cys Leu Arg Ser Glu Gly Ser Pro Leu Val Val
225                 230                 235                 240

Leu Pro Tyr Met Lys His Gly Asp Leu Arg Asn Phe Ile Arg Asn Glu
                245                 250                 255

Thr His Asn Pro Thr Val Lys Asp Leu Ile Gly Phe Gly Leu Gln Val
            260                 265                 270

Ala Lys Gly Met Lys Tyr Leu Ala Ser Lys Lys Phe Val His Arg Asp
        275                 280                 285

Leu Ala Ala Arg Asn Cys Met Leu Asp Glu Lys Phe Thr Val Lys Val
    290                 295                 300

Ala Asp Phe Gly Leu Ala Arg Asp Met Tyr Asp Lys Glu Tyr Tyr Ser
305                 310                 315                 320

Val His Asn Lys Thr Gly Ala Lys Leu Pro Val Lys Trp Met Ala Leu
                325                 330                 335

Glu Ser Leu Gln Thr Gln Lys Phe Thr Thr Lys Ser Asp Val Trp Ser
            340                 345                 350

Phe Gly Val Leu Leu Trp Glu Leu Met Thr Arg Gly Ala Pro Pro Tyr
        355                 360                 365

Pro Asp Val Asn Thr Phe Asp Ile Thr Val Tyr Leu Leu Gln Gly Arg
    370                 375                 380

Arg Leu Leu Gln Pro Glu Tyr Cys Pro Asp Pro Leu Tyr Glu Val Met
385                 390                 395                 400

Leu Lys Cys Trp His Pro Lys Ala Glu Met Arg Pro Ser Phe Ser Glu
                405                 410                 415

Leu Val Ser Arg Ile Ser Ala Ile Phe Ser Thr Phe Ile Gly Glu His
            420                 425                 430
```

Tyr Val His Val Asn Ala Thr Tyr Val Asn Val Lys Cys Val Ala Pro
435 440 445

Tyr Pro Ser Leu Leu Ser Ser Glu Asp Asn Ala Asp Asp Glu Val Asp
450 455 460

Thr Arg Pro Ala Ser Phe Trp Glu Thr Ser
465 470

<210> 3
<211> 315
<212> PRT
<213> Unknown

<220>
<223> KDR protein sequence used for screening

<400> 3

Asp Pro Asp Glu Leu Pro Leu Asp Glu His Cys Glu Arg Leu Pro Tyr
1 5 10 15

Asp Ala Ser Lys Trp Glu Phe Pro Arg Asp Arg Leu Lys Leu Gly Lys
20 25 30

Pro Leu Gly Arg Gly Ala Phe Gly Gln Val Ile Glu Ala Asp Ala Phe
35 40 45

Gly Ile Asp Lys Thr Ala Thr Cys Arg Thr Val Ala Val Lys Met Leu
50 55 60

Lys Glu Gly Ala Thr His Ser Glu His Arg Ala Leu Met Ser Glu Leu
65 70 75 80

Lys Ile Leu Ile His Ile Gly His His Leu Asn Val Val Asn Leu Leu
85 90 95

Gly Ala Cys Thr Lys Pro Gly Gly Pro Leu Met Val Ile Val Glu Phe
100 105 110

Cys Lys Phe Gly Asn Leu Ser Thr Tyr Leu Arg Ser Lys Arg Asn Glu
115 120 125

Phe Val Pro Tyr Lys Val Ala Pro Glu Asp Leu Tyr Lys Asp Phe Leu
130 135 140

Thr Leu Glu His Leu Ile Cys Tyr Ser Phe Gln Val Ala Lys Gly Met
145 150 155 160

```
Glu Phe Leu Ala Ser Arg Lys Cys Ile His Arg Asp Leu Ala Ala Arg
                165                 170                 175

Asn Ile Leu Leu Ser Glu Lys Asn Val Val Lys Ile Cys Asp Phe Gly
            180                 185                 190

Leu Ala Arg Asp Ile Tyr Lys Asp Pro Asp Tyr Val Arg Lys Gly Asp
        195                 200                 205

Ala Arg Leu Pro Leu Lys Trp Met Ala Pro Glu Thr Ile Phe Asp Arg
    210                 215                 220

Val Tyr Thr Ile Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu Trp
225                 230                 235                 240

Glu Ile Phe Ser Leu Gly Ala Ser Pro Tyr Pro Gly Val Lys Ile Asp
                245                 250                 255

Glu Glu Phe Cys Arg Arg Leu Lys Glu Gly Thr Arg Met Arg Ala Pro
            260                 265                 270

Asp Tyr Thr Thr Pro Glu Met Tyr Gln Thr Met Leu Asp Cys Trp His
        275                 280                 285

Gly Glu Pro Ser Gln Arg Pro Thr Phe Ser Glu Leu Val Glu His Leu
    290                 295                 300

Gly Asn Leu Leu Gln Ala Asn Ala Gln Gln Asp
305                 310                 315


<210>  4
<211>  435
<212>  PRT
<213>  Unknown

<220>
<223>  cFMS protein sequence used for screening

<400>  4

Tyr Lys Tyr Lys Gln Lys Pro Lys Tyr Gln Val Arg Trp Lys Ile Ile
1               5                   10                  15

Glu Ser Tyr Glu Gly Asn Ser Tyr Thr Phe Ile Asp Pro Thr Gln Leu
            20                  25                  30

Pro Tyr Asn Glu Lys Trp Glu Phe Pro Arg Asn Asn Leu Gln Phe Gly
        35                  40                  45
```

```
Lys Thr Leu Gly Ala Gly Ala Phe Gly Lys Val Val Glu Ala Thr Ala
    50                  55                  60

Phe Gly Leu Gly Lys Glu Asp Ala Val Leu Lys Val Ala Val Lys Met
65                  70                  75                  80

Leu Lys Ser Thr Ala His Ala Asp Glu Lys Glu Ala Leu Met Ser Glu
                85                  90                  95

Leu Lys Ile Met Ser His Leu Gly Gln His Glu Asn Ile Val Asn Leu
            100                 105                 110

Leu Gly Ala Cys Thr His Gly Gly Pro Val Leu Val Ile Thr Glu Tyr
        115                 120                 125

Cys Cys Tyr Gly Asp Leu Leu Asn Phe Leu Arg Arg Lys Ala Glu Ala
    130                 135                 140

Met Leu Gly Pro Ser Leu Ser Pro Gly Gln Asp Pro Glu Gly Gly Val
145                 150                 155                 160

Asp Tyr Lys Asn Ile His Leu Glu Lys Lys Tyr Val Arg Arg Asp Ser
                165                 170                 175

Gly Phe Ser Ser Gln Gly Val Asp Thr Tyr Val Glu Met Arg Pro Val
            180                 185                 190

Ser Thr Ser Ser Asn Asp Ser Phe Ser Glu Gln Asp Leu Asp Lys Glu
        195                 200                 205

Asp Gly Arg Pro Leu Glu Leu Arg Asp Leu Leu His Phe Ser Ser Gln
    210                 215                 220

Val Ala Gln Gly Met Ala Phe Leu Ala Ser Lys Asn Cys Ile His Arg
225                 230                 235                 240

Asp Val Ala Ala Arg Asn Val Leu Leu Thr Asn Gly His Val Ala Lys
                245                 250                 255

Ile Gly Asp Phe Gly Leu Ala Arg Asp Ile Met Asn Asp Ser Asn Tyr
            260                 265                 270

Ile Val Lys Gly Asn Ala Arg Leu Pro Val Lys Trp Met Ala Pro Glu
        275                 280                 285

Ser Ile Phe Asp Cys Val Tyr Thr Val Gln Ser Asp Val Trp Ser Tyr
    290                 295                 300
```

```
Gly Ile Leu Leu Trp Glu Ile Phe Ser Leu Gly Leu Asn Pro Tyr Pro
305                 310                 315                 320

Gly Ile Leu Val Asn Ser Lys Phe Tyr Lys Leu Val Lys Asp Gly Tyr
                325                 330                 335

Gln Met Ala Gln Pro Ala Phe Ala Pro Lys Asn Ile Tyr Ser Ile Met
            340                 345                 350

Gln Ala Cys Trp Ala Leu Glu Pro Thr His Arg Pro Thr Phe Gln Gln
        355                 360                 365

Ile Cys Ser Phe Leu Gln Glu Gln Ala Gln Glu Asp Arg Arg Glu Arg
    370                 375                 380

Asp Tyr Thr Asn Leu Pro Ser Ser Ser Arg Ser Gly Gly Ser Gly Ser
385                 390                 395                 400

Ser Ser Ser Glu Leu Glu Glu Glu Ser Ser Ser Glu His Leu Thr Cys
                405                 410                 415

Cys Glu Gln Gly Asp Ile Ala Gln Pro Leu Leu Gln Pro Asn Asn Tyr
            420                 425                 430

Gln Phe Cys
        435
```