

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent No. 6,011,068  
Issue date January 4, 2000  
Inventors Edward F. Nemeth, Bradford C. Van Wagenen, Manuel F. Balandrin, Eric G. DelMar, Scott T. Moe  
For CALCIUM RECEPTOR-ACTIVE MOLECULES

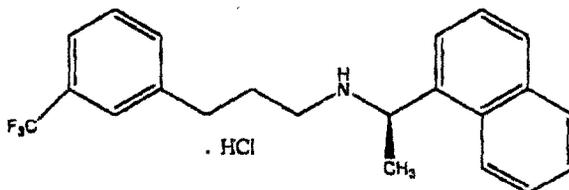
Hon. Commissioner of Patents and Trademarks  
Box Patent Extensions  
Washington, DC 20231

Dear Sir:

APPLICATION FOR EXTENSION OF PATENT TERM UNDER 35 U.S.C. 156

Applicants NPS Pharmaceuticals Inc., a Delaware Corporation and Brigham & Women's Hospital, represent that they are the co-assignees of the entire interest in and to Letters Patent of the United States No. 6,011,068 granted to Nemeth, et al. on January 4, 2000. The assignment from inventors to NPS Pharmaceuticals, Inc. was recorded on February 10, 1995, Reel 7384, Frame 0691. The assignment from inventors to The Brigham & Women's Hospital was recorded on February 10, 1995, Reel 7384, Frame 0696. Applicants hereby submit this application for an extension of patent term under 35 U.S.C. 156 by providing the following information as required by §1.740 of Title 37 of the code of Federal Regulations (37 CFR 1.740).

1. The approved product is SENSIPAR™, a trademark owned by Amgen Inc., for cinacalcet hydrochloride which is N-[1-(R)-(1-naphthyl)ethyl]-3-[3-(trifluoromethyl)phenyl]-1-aminopropane hydrochloride and has the following structure:



The product has the following physical characteristics:

023.250710v1

2004E-0446

APP/

Molecular weight: 393.9 g/mol

Empirical formula:  $C_{22}H_{22}F_3N \cdot HCl$

2. The approved product was subject to regulatory reviews under Section 505 of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. 355.
3. The approved product SENSIPAR™ (cinacalcet hydrochloride) received permission for commercial marketing or use under §505 of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. 355, on March 8, 2004.
4. The active ingredient in the approved product SENSIPAR™ is cinacalcet hydrochloride which has not been previously approved for commercial marketing or use under the Federal Food, Drug and Cosmetic Act, the Public Health Service Act, or the Virus-Serum-Toxin Act. No other active ingredients are contained in the product.
5. This application for extension of patent term under 35 U.S.C. 156 is being submitted within the sixty (60) day period permitted for submission pursuant to §1.720(f). The last day for submitting an application for extension is May 7, 2004.
6. The complete identification of the patent for which an extension is being sought is as follows:

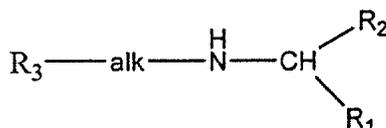
|                 |  |
|-----------------|--|
| Inventors       | Edward F. Nemeth, Bradford C. Van Wagenen, Manuel F. Balandrin, Eric G. DelMar, Scott T. Moe |
| Patent No.      | 6,011,068  |
| Issue date      | January 4, 2000  |
| Expiration date | December 14, 2016 (subject to terminal disclaimer)   |
7. A copy of the patent for which an extension is being sought is attached hereto as Attachment "A".
8. U.S. Patent 6,011,068 issued on January 4, 2000 and the first maintenance fee was due during the period from January 4, 2003 to July 4, 2003. A receipt of maintenance fee payment was received on July 11, 2003, and a copy is attached hereto as Attachment B. This patent is subject to a terminal disclaimer and a copy is attached hereto as Attachment C. Certificates of

Correction that have been issued with respect to U.S. Patent No. 6,011,068 were issued on: December 4, 2001, January 29, 2002 and February 25, 2003, copies of which are attached hereto as Attachment D. An additional Certificate of Correction was also filed on May 6, 2004, a copy of which his attached hereto as Attachment E.

9. The patent claims the approved product SENSIPAR™ (cinacalcet hydrochloride) in claims 1-3, 5-7, 21, 26, 28-29, 32, 37, 61-62, 67-68, 73-75, 77, 79-84, 90-91, and 100 (included below).

**Claim 1 generically claims cinacalcet hydrochloride, where R<sub>3</sub> is phenyl substituted with CF<sub>3</sub>, alk is n-propylene, R<sub>2</sub> is naphthyl, R<sub>1</sub> is methyl, and the pharmaceutically acceptable acid addition salt or complex is hydrochloride.**

Claim 1. A compound having the chemical formula:



wherein alk is selected from the group consisting of n-propylene, 2,4-butylene and 1,3-butylene;

R<sub>1</sub> is lower alkyl of from 1 to 3 carbon atoms or lower haloalkyl of from 1 to 3 carbon atoms substituted with from 1 to 7 halogen atoms; and

R<sub>2</sub> and R<sub>3</sub> are independently selected monocyclic or bicyclic carbocyclic aryl or cycloalkyl groups, having 5- to 7-membered rings optionally substituted with 1 to 5 substituents independently selected from the group consisting of: OCF<sub>3</sub>, lower alkyl of 1 to 3 carbon atoms, lower haloalkyl of 1 to 3 carbon atoms substituted with 1 to 7 halogen atoms, lower alkoxy of 1 to 3 carbon atoms, halogen, nitro, amino, alkylamino, amido, lower alkylamido of 1 to 3 carbon atoms, cyano, hydroxy, acyl of 2 to 4 carbon atoms, lower hydroxyalkyl of 1 to 3 carbon atoms, and lower thioalkyl of 1 to 3 carbon atoms; provided that if R<sub>2</sub> is phenyl, then said phenyl R<sub>2</sub> has at least one substituent and is not 4-OH-phenyl; or a pharmaceutically acceptable acid addition salt or complex thereof.

**Claim 2 generically claims cinacalcet hydrochloride, where R<sub>3</sub> is phenyl substituted with CF<sub>3</sub>, alk is n-propylene, R<sub>2</sub> is naphthyl, R<sub>1</sub> is methyl, and the pharmaceutically acceptable acid addition salt or complex is hydrochloride.**

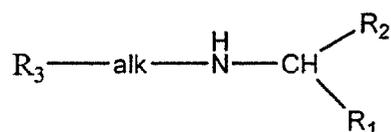
Claim 2. The compound of claim 1 wherein alk is n-propylene.

**Claim 3 generically claims cinacalcet hydrochloride, where R<sub>3</sub> is phenyl substituted with CF<sub>3</sub>, alk is n-propylene, R<sub>2</sub> is naphthyl, R<sub>1</sub> is methyl, and the pharmaceutically acceptable acid addition salt or complex is hydrochloride.**

Claim 3. The compound of claim 2 wherein R<sub>1</sub> is methyl.

**Claim 5 generically claims cinacalcet hydrochloride, where R<sub>3</sub> is phenyl substituted with CF<sub>3</sub>, alk is n-propylene, R<sub>2</sub> is naphthyl, R<sub>1</sub> is methyl, and the pharmaceutically acceptable acid addition salt or complex is hydrochloride.**

Claim 5. A compound having the chemical formula:



wherein alk is either n-propylene, 2,4-butylene, or 1,3-butylene; R<sub>1</sub> is a lower alkyl of from 1 to 3 carbon atoms;

R<sub>2</sub> is either naphthyl or a phenyl substituted with 1 to 5 substituents, and R<sub>3</sub> is either cyclohexyl, naphthyl, or a phenyl optionally substituted with 1 to 5 substituents; wherein each of said R<sub>2</sub> substituents and each of said R<sub>3</sub> substituents are independently selected from the group consisting of: OCF<sub>3</sub>, lower alkyl of 1 to 3 carbon atoms, lower haloalkyl of 1 to 3 carbon atoms substituted with 1 to 7 halogen atoms, lower alkoxy of 1 to 3 carbon atoms, halogen, nitro, amino, alkylamino, amido, lower alkylamido of 1 to 3 carbon atoms, cyano, hydroxy, acyl of 2 to 4 carbon atoms, lower hydroxyalkyl of 1 to 3 carbon atoms, and lower thioalkyl of 1 to 3 carbon atoms;

provided that R<sub>2</sub> is not 4-OH-phenyl; or

a pharmaceutically acceptable acid addition salt or complex thereof.

**Claim 6 generically claims cinacalcet hydrochloride, where R<sub>3</sub> is phenyl substituted with CF<sub>3</sub>, alk is n-propylene, R<sub>2</sub> is naphthyl, R<sub>1</sub> is methyl, and the pharmaceutically acceptable acid addition salt or complex is hydrochloride.**

Claim 6. The compound of claim 5, wherein

R<sub>1</sub> is methyl; and

each of said R<sub>2</sub> substituents and each of said R<sub>3</sub> substituents are independently selected from the group consisting of: lower alkyl of 1 to 3 carbon atoms, lower haloalkyl of 1 to 3 carbon atoms substituted with 1 to 7 halogen atoms, lower alkoxy of 1 to 3 carbon atoms, halogen, nitro,

amino, amido, lower alkylamido of 1 to 3 carbon atoms, cyano, acyl of 2 to 4 carbon atoms, lower hydroxyalkyl of 1 to 3 carbon atoms, and lower thioalkyl of 1 to 3 carbon atoms.

**Claim 7 generically claims cinacalcet hydrochloride, where R<sub>3</sub> is phenyl substituted with CF<sub>3</sub>, alk is n-propylene, R<sub>2</sub> is naphthyl, R<sub>1</sub> is methyl, and the pharmaceutically acceptable acid addition salt or complex is hydrochloride.**

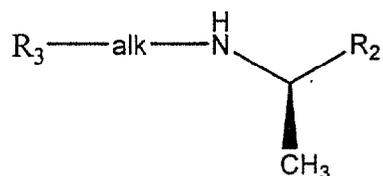
Claim 7. The compound of claim 6, wherein

R<sub>2</sub> is either naphthyl or said phenyl having 1 to 5 substituents; and

R<sub>3</sub> is either naphthyl or said phenyl optionally substituted with 1 to 5 substituents.

**Claim 21 generically claims cinacalcet hydrochloride, where R<sub>3</sub> is phenyl substituted with CF<sub>3</sub>, alk is n-propylene, R<sub>2</sub> is naphthyl, and the pharmaceutically acceptable acid addition salt or complex is hydrochloride.**

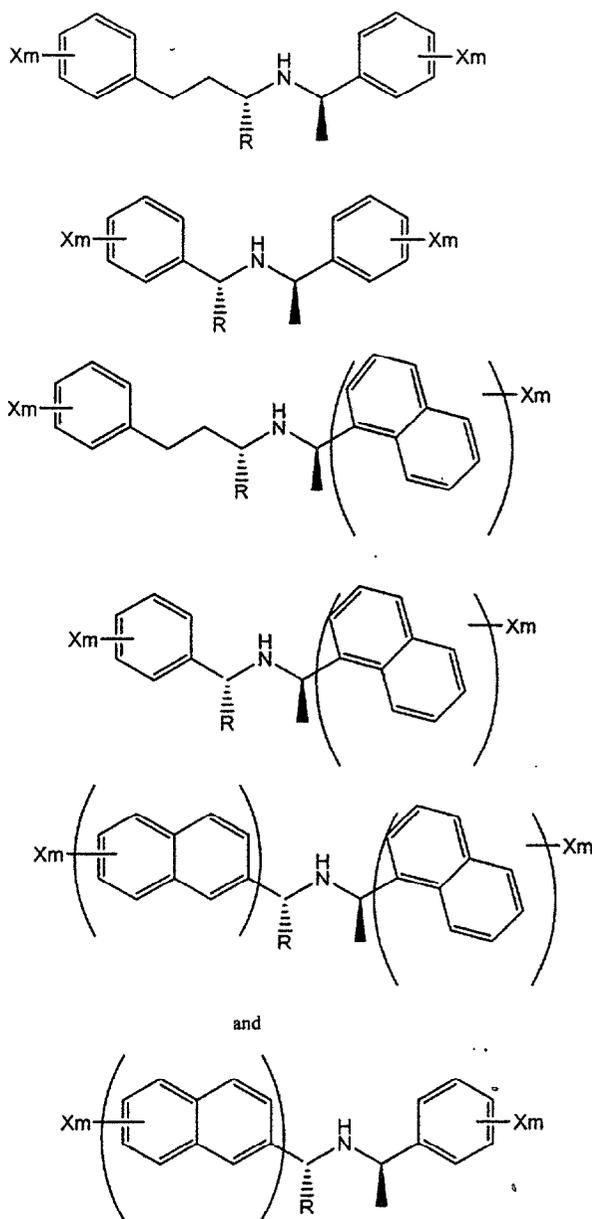
Claim 21. The compound of any one of claims 5-7, wherein said compound is an R enantiomer having the following chemical structure:



or a pharmaceutically acceptable acid addition salt or complex thereof.

**Claim 26 generically claims cinacalcet hydrochloride, because cinacalcet hydrochloride is a compound of the first listed formula where m is 1 on the phenyl ring, X is CF<sub>3</sub> on the phenyl ring, R is hydrogen, m is 0 on the naphthyl ring, and the pharmaceutically acceptable acid addition salt or complex is hydrochloride.**

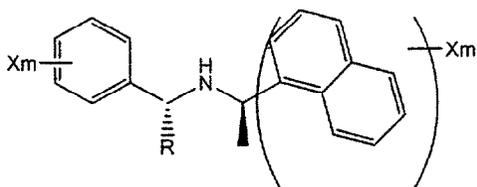
Claim 26. A compound represented by a formula selected from the group consisting of



wherein  $m$  is independently an integer of 0 to 5 for naphthyl rings and  $m$  is independently an integer of 1 to 5 for phenyl rings;

$X$  is independently selected from the group consisting of --Br, --Cl, --F, --I, --CN, --NO<sub>2</sub>, --OR, --NR<sub>2</sub>, --CF<sub>3</sub>, --SR, --S(O)R, --S(O)<sub>2</sub>R, --C(O)R, --OC(O)R, --C(O)OR, --NRC(O)R, C(O)NR<sub>2</sub>, methyl and isopropyl radicals; provided that the  $X$  substituent on the phenyl ring of the Ph-CHR-group is other than hydroxy, 4-OCH<sub>3</sub>, or 4-CH<sub>3</sub>; and

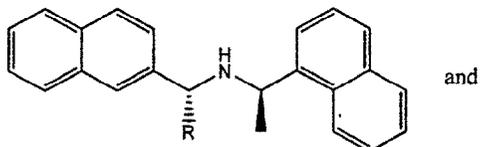
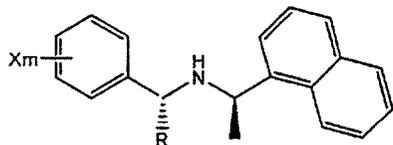
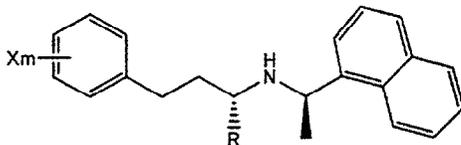
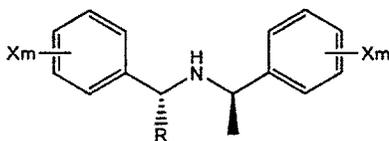
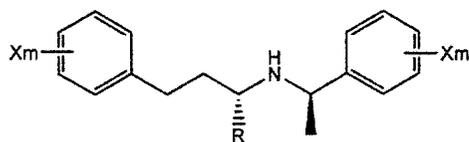
each  $R$  is independently either a hydrogen, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl, C<sub>2</sub>-C<sub>10</sub> alkynyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, --CF<sub>3</sub>, --CF<sub>2</sub>H, --CFH<sub>2</sub>, --CH<sub>2</sub>CF<sub>3</sub> or phenyl radical; provided that if said compound has the chemical formula:



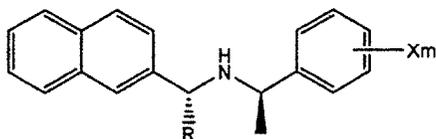
wherein the naphthyl is either unsubstituted or substituted with a lower alkyl or halogen and only one substituent is present on the phenyl, then said one substituent is not lower alkyl or halogen; or a pharmaceutically acceptable acid addition salt or complex thereof.

**Claim 28 generically claims cinacalcet hydrochloride, where m is 1, X is CF<sub>3</sub>, R is hydrogen, and the pharmaceutically acceptable acid addition salt or complex is hydrochloride in the third structure shown.**

Claim 28. The compound of claim 26, represented by a formula selected from the group consisting of:



and



wherein each m is independently an integer of 1 to 5;

each X is independently selected from the group consisting of --Cl, --F, --I, --CF<sub>3</sub>, --OCF<sub>3</sub>, --OCH<sub>2</sub>CF<sub>3</sub>, --SCH<sub>3</sub>, methyl, isopropyl and methoxy radicals; and

R is a hydrogen, methyl, ethyl or isopropyl radical; or a pharmaceutically acceptable acid addition salt or complex thereof.

**Claim 29 generically claims cinacalcet hydrochloride, where m is 1, X is CF<sub>3</sub>, R is hydrogen, and the pharmaceutically acceptable acid addition salt or complex is hydrochloride.**

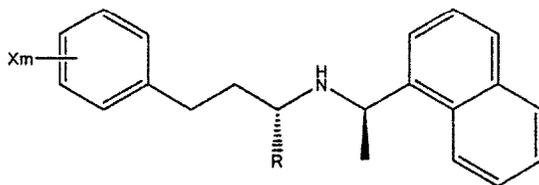
Claim 29. The compound of claim 28, wherein each m is independently an integer of 1 or 2;

X is independently selected from the group consisting of --Cl, --F, --CF<sub>3</sub>, --SCH<sub>3</sub>, methyl and methoxy radicals, and

R is a hydrogen or methyl radical.

**Claim 32 generically claims cinacalcet hydrochloride, where m is 1, X is CF<sub>3</sub>, R is hydrogen, and the pharmaceutically acceptable acid addition salt or complex is hydrochloride.**

Claim 32. The compound of claim 29, wherein said compound has the following formula:



or a pharmaceutically acceptable acid addition salt or complex thereof.

**Claim 37 generically claims a pharmaceutical composition comprising cinacalcet hydrochloride, where m on the phenyl ring is 1, X on the phenyl ring is CF<sub>3</sub>, m on the naphthyl ring (when present) is 0, R is hydrogen, and the pharmaceutically acceptable acid addition salt or complex is hydrochloride.**

Claim 37. A pharmaceutical composition comprising the compound of any one of claims 26-29 and 30-36, and a pharmaceutically acceptable carrier.

**Claim 61 generically claims cinacalcet hydrochloride, where R<sub>3</sub> is phenyl substituted with CF<sub>3</sub>, alk is n-propylene, R<sub>2</sub> is naphthyl, R<sub>1</sub> is methyl, and the pharmaceutically acceptable salt is hydrochloride, and a pharmaceutically acceptable carrier.**

Claim 61. The compound of claim 5, wherein

R<sub>1</sub> is methyl; and

each of said R<sub>2</sub> substituents and each of said R<sub>3</sub> substituents are independently selected from the group consisting of: OCF<sub>3</sub>, lower alkyl of 1 to 3 carbon atoms, lower haloalkyl of 1 to 3 carbon atoms substituted with 1 to 7 halogen atoms, lower alkoxy of 1 to 3 carbon atoms, halogen, nitro, amino, alkylamino, amido, lower alkylamido of 1 to 3 carbon atoms, cyano, acyl of 2 to 4 carbon atoms, lower hydroxyalkyl of 1 to 3 carbon atoms, and lower thioalkyl of 1 to 3 carbon atoms.

**Claim 62 generically claims cinacalcet hydrochloride, where R<sub>3</sub> is phenyl substituted with CF<sub>3</sub>, alk is n-propylene, R<sub>2</sub> is naphthyl, R<sub>1</sub> is methyl, and the pharmaceutically acceptable salt is hydrochloride, and a pharmaceutically acceptable carrier.**

Claim 62. The compound of claim 61, wherein alk is n-propylene.

**Claim 67 generically claims cinacalcet hydrochloride, where R<sub>3</sub> is phenyl substituted with CF<sub>3</sub>, alk is n-propylene, R<sub>2</sub> is naphthyl, R<sub>1</sub> is methyl, and the pharmaceutically acceptable salt is hydrochloride, and a pharmaceutically acceptable carrier.**

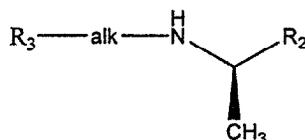
Claim 67. The compound of any one of claims 61-65, wherein R<sub>3</sub> is said optionally substituted phenyl.

**Claim 68 generically claims cinacalcet hydrochloride, where R<sub>3</sub> is phenyl substituted with CF<sub>3</sub>, alk is n-propylene, R<sub>2</sub> is naphthyl, R<sub>1</sub> is methyl, and the pharmaceutically acceptable salt is hydrochloride, and a pharmaceutically acceptable carrier.**

Claim 68. The compound of claim 67, wherein R<sub>2</sub> is naphthyl.

**Claim 73 generically claims cinacalcet hydrochloride, where R<sub>3</sub> is phenyl substituted with CF<sub>3</sub>, alk is n-propylene, R<sub>2</sub> is naphthyl, and the pharmaceutically acceptable salt is hydrochloride.**

Claim 73. The compound of any one of claims 61-65, wherein said compound is an enantiomer having the following chemical structure:



or a pharmaceutically acceptable acid addition salt or complex thereof.

**Claim 74 generically claims cinacalcet hydrochloride, where  $R_3$  is phenyl substituted with  $CF_3$ , alk is n-propylene,  $R_2$  is naphthyl, and the pharmaceutically acceptable salt is hydrochloride, and cinacalcet hydrochloride causes an increase in  $(Ca^{2+})_i$  with an  $EC_{50}$  less than or equal to 5  $\mu M$  as determined by measuring  $(Ca^{2+})_i$  in bovine parathyroid cells loaded with fura-2 using the Cytosolic  $Ca^{2+}$  Cell Assay.**

Claim 74. The compound of claim 73, wherein said compound causes an increase in  $(Ca^{2+})_i$  with an  $EC_{50}$  less than or equal to 5  $\mu M$  as determined by measuring  $(Ca^{2+})_i$  in bovine parathyroid cells loaded with fura-2 using the Cytosolic  $Ca^{2+}$  Cell Assay.

**Claim 75 generically claims a composition comprising cinacalcet hydrochloride, where  $R_3$  is phenyl substituted with  $CF_3$ , alk is a straight chain alkylene of 3 carbon atoms,  $R_2$  is naphthyl, and the pharmaceutically acceptable salt is hydrochloride, and cinacalcet hydrochloride causes an increase in  $(Ca^{2+})_i$  with an  $EC_{50}$  less than or equal to 5  $\mu M$  as determined by measuring  $(Ca^{2+})_i$  in bovine parathyroid cells loaded with fura-2 using the Cytosolic  $Ca^{2+}$  Cell Assay.**

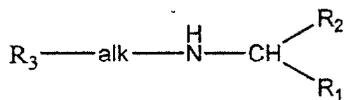
Claim 75. The pharmaceutical composition of claim 100, wherein said compound causes an increase in  $(Ca^{2+})_i$  with an  $EC_{50}$  less than or equal to 5  $\mu M$  as determined by measuring  $(Ca^{2+})_i$  in bovine parathyroid cells loaded with fura-2 using the Cytosolic  $Ca^{2+}$  Cell assay.

**Claim 77 generically claims cinacalcet hydrochloride, where  $R_3$  is phenyl substituted with  $CF_3$ , alk is n-propylene,  $R_2$  is naphthyl, and the pharmaceutically acceptable salt is hydrochloride, and cinacalcet hydrochloride causes an increase in  $(Ca^{2+})_i$  with an  $EC_{50}$  less than or equal to 5  $\mu M$  as determined by measuring  $(Ca^{2+})_i$  in bovine parathyroid cells loaded with fura-2 using the Cytosolic  $Ca^{2+}$  Cell Assay.**

Claim 77. The compound of claim 21, wherein said compound causes an increase in  $(Ca^{2+})_i$  with an  $EC_{50}$  less than or equal to 5  $\mu M$  as determined by measuring  $(Ca^{2+})_i$  in bovine parathyroid cells loaded with fura-2 using the Cytosolic  $Ca^{2+}$  Cell Assay.

**Claim 79 generically claims a pharmaceutical composition comprising cinacalcet hydrochloride, where  $R_3$  is phenyl substituted with  $CF_3$ , alk is a straight chain alkylene of 3 carbon atoms,  $R_2$  is naphthyl,  $R_1$  is methyl, and the pharmaceutically acceptable salt is hydrochloride.**

Claim 79. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound having the chemical formula:



wherein

alk is a straight- or branched-chain alkylene of from 0 to 6 carbon atoms;

R<sub>1</sub> is a lower alkyl of from 1 to 3 carbon atoms or a lower haloalkyl of from 1 to 3 carbon atoms substituted with from 1 to 7 halogen atoms; and

R<sub>2</sub> and R<sub>3</sub> are each independently selected monocyclic or bicyclic carbocyclic aryl or cycloalkyl groups, having 5- to 7-membered rings optionally substituted with 1 to 5 substituents each independently selected from the group consisting of: OCF<sub>3</sub>, lower alkyl of 1 to 3 carbon atoms, lower haloalkyl of 1 to 3 carbon atoms substituted with 1 to 7 halogen atoms, lower alkoxy of 1 to 3 carbon atoms, halogen, nitro, amino, alkylamino, amido, lower alkylamido of 1 to 3 carbon atoms, cyano, hydroxy, acyl of 2 to 4 carbon atoms, lower hydroxyalkyl of 1 to 3 carbon atoms, and lower thioalkyl of 1 to 3 carbon atoms; provided that if R<sub>2</sub> is phenyl, then R<sub>2</sub> is substituted with 1 to 5 substituents; further provided that if R<sub>3</sub> is cycloalk and alk is --CH<sub>2</sub>--, then R<sub>2</sub> is not 4 aminophenyl; or a pharmaceutically acceptable acid addition salt or complex thereof.

**Claim 80 generically claims a pharmaceutical composition comprising cinacalcet hydrochloride, where R<sub>3</sub> is phenyl substituted with CF<sub>3</sub>, alk is a straight chain alkylene of 3 carbon atoms, R<sub>2</sub> is naphthyl, R<sub>1</sub> is methyl, and the pharmaceutically acceptable salt is hydrochloride.**

Claim 80. The pharmaceutical composition of claim 79, wherein alk is 1 to 6 carbon atoms;

R<sub>1</sub> is lower alkyl of from 1 to 3 carbon atoms; and

R<sub>2</sub> is either naphthyl or a substituted phenyl having 1 to 5 substituents, and R<sub>3</sub> is either cyclohexyl, naphthyl, or a phenyl optionally substituted with 1 to 5 substituents, wherein each R<sub>2</sub> and R<sub>3</sub> substituent is independently selected from the group consisting of: OCF<sub>3</sub>, lower alkyl of 1 to 3 carbon atoms, lower haloalkyl of 1 to 3 carbon atoms substituted with 1 to 7 halogen atoms, lower alkoxy of 1 to 3 carbon atoms, halogen, nitro, amino, alkylamino, amido, lower alkylamido of 1 to 3 carbon atoms, cyano, hydroxy, acyl of 2 to 4 carbon atoms, lower hydroxyalkyl of 1 to 3 carbon atoms, and lower thioalkyl of 1 to 3 carbon atoms.

**Claim 81 generically claims a pharmaceutical composition comprising cinacalcet hydrochloride, where R<sub>3</sub> is phenyl substituted with CF<sub>3</sub>, alk is a straight chain alkylene of 3 carbon atoms, R<sub>2</sub> is naphthyl, R<sub>1</sub> is methyl, and the pharmaceutically acceptable salt is hydrochloride.**

Claim 81. The pharmaceutical composition of claim 79, wherein alk is 1 to 6 carbon atoms;

R<sub>1</sub> is lower alkyl of from 1 to 3 carbon atoms;

R<sub>2</sub> is either naphthyl or a substituted phenyl having 1 to 5 substituents each independently selected from the group consisting of: lower alkyl of 1 to 3 carbon atoms, lower haloalkyl of 1 to 3 carbon atoms substituted with 1 to 7 halogen atoms, lower alkoxy of 1 to 3 carbon atoms, halogen, nitro, amino, alkylamino, amido, lower alkylamido of 1 to 3 carbon atoms, cyano, hydroxy, acyl of 2 to 4 carbon atoms, lower hydroxyalkyl of 1 to 3 carbon atoms, and lower thioalkyl of 1 to 3 carbon atoms; and

R<sub>3</sub> is either cyclohexyl, naphthyl, or a phenyl optionally substituted with 1 to 5 substituents each independently selected from the group consisting of: lower alkyl of 1 to 3 carbon atoms, lower haloalkyl of 1 to 3 carbon atoms substituted with 1 to 7 halogen atoms, lower alkoxy of 1 to 3 carbon atoms, halogen, nitro, amino, alkylamino, amido, lower alkylamido of 1 to 3 carbon atoms, cyano, hydroxy, acyl of 2 to 4 carbon atoms, lower hydroxyalkyl of 1 to 3 carbon atoms, and lower thioalkyl of 1 to 3 carbon atoms.

**Claim 82 generically claims a pharmaceutical composition comprising cinacalcet hydrochloride, where R<sub>3</sub> is phenyl substituted with CF<sub>3</sub>, alk is a straight chain alkylene of 3 carbon atoms, R<sub>2</sub> is naphthyl, R<sub>1</sub> is methyl, and the pharmaceutically acceptable salt is hydrochloride.**

Claim 82. The pharmaceutical composition of claim 81, wherein alk is an alkylene chain 1 to 3 carbon atoms in length which may be substituted with a methyl.

**Claim 83 generically claims a pharmaceutical composition comprising cinacalcet hydrochloride, where R<sub>3</sub> is phenyl substituted with CF<sub>3</sub>, alk is a straight chain alkylene of 3 carbon atoms, R<sub>2</sub> is naphthyl, R<sub>1</sub> is methyl, and the pharmaceutically acceptable salt is hydrochloride.**

Claim 83. The pharmaceutical composition of claim 81, wherein R<sub>1</sub> is methyl.

**Claim 84 generically claims a pharmaceutical composition comprising cinacalcet hydrochloride, where R<sub>3</sub> is phenyl substituted with CF<sub>3</sub>, alk is n-propylene, R<sub>2</sub> is naphthyl, R<sub>1</sub> is methyl, and the pharmaceutically acceptable salt is hydrochloride.**

Claim 84. The pharmaceutical composition of claim 83, wherein alk is n-propylene.

**Claim 90 generically claims a pharmaceutical composition comprising cinacalcet hydrochloride, where R<sub>3</sub> is phenyl substituted with CF<sub>3</sub>, alk is n-propylene, R<sub>2</sub> is naphthyl, R<sub>1</sub> is methyl, and the pharmaceutically acceptable salt is hydrochloride.**

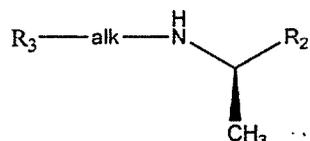
Claim 90. The pharmaceutical composition of any one of claims 84 -88, wherein R<sub>3</sub> is said optionally substituted phenyl.

**Claim 91 generically claims a pharmaceutical composition comprising cinacalcet hydrochloride, where R<sub>3</sub> is phenyl substituted with CF<sub>3</sub>, alk is n-propylene, R<sub>2</sub> is naphthyl, R<sub>1</sub> is methyl, and the pharmaceutically acceptable salt is hydrochloride.**

Claim 91. The pharmaceutical composition of claim 90, wherein R<sub>2</sub> is naphthyl.

**Claim 100 generically claims a pharmaceutical composition comprising cinacalcet hydrochloride, where R<sub>3</sub> is phenyl substituted with CF<sub>3</sub>, alk is an alkylene chain of 3 carbon atoms, R<sub>2</sub> is naphthyl, and the pharmaceutically acceptable salt is hydrochloride, and cinacalcet hydrochloride is an R enantiomer.**

Claim 100. The pharmaceutical composition of any one of claims 80 -83, wherein said compound is an R enantiomer having the following chemical structure:



or a pharmaceutically acceptable acid addition salt or complex thereof.

10. The relevant dates and information pursuant to 35 U.S.C. 156(g) to enable the Secretary of Health and Human Services to determine the applicable regulatory review period are as follows:

- (i) the effective date of the investigational new drug (IND) application was June 19, 1998;
- (ii) the IND number was 56,010;
- (iii) the date on which a new drug application (NDA) was initially submitted was September 5, 2003;
- (iv) the NDA number was 21-688; and
- (v) the date on which the NDA was approved was March 8, 2004.

11. The following is a brief description of the significant activities undertaken by the marketing applicant (Amgen Inc.) during the applicable regulatory review period with respect to SENSIPAR™ (cinacalcet hydrochloride) and the significant dates applicable to such activities:

- (i) the effective date of the IND filing was June 19, 1998;
- (ii) the clinical trials were performed in subjects having secondary hyperparathyroidism, primary hyperparathyroidism and parathyroid carcinoma;
- (iii) the NDA application was submitted September 5, 2003 and expedited review was granted by the FDA; and
- (iv) the NDA was approved on March 8, 2004.
- (v) additional activities undertaken during the applicable regulatory review period are described in a list, attached hereto as Attachment F.

12(A). It is the opinion of the Applicants that U.S. Patent No. 6,011,068 claims a product that has undergone a regulatory review which would be considered in determining any extension for patent under 35 U.S.C. 156 for the following reasons:

- (i) U.S. Patent No. 6,011,068 claims a product (35 U.S.C. 156(a));
- (ii) The term of U.S. Patent No. 6,011,068 has not expired before submission of this application for an extension (35 U.S.C. 156(a)(1));
- (iii) The term of U.S. Patent No. 6,011,068 has never been previously extended (35 U.S.C. 156(a)(2));
- (iv) The application for extension is submitted by the owners of record of U.S. Patent No. 6,011,068 in accordance with the requirements of 35 U.S.C. 156(d), 37 CFR 1.730, and 37 CFR 1.740 (35 U.S.C. 156(a)(3));
- (v) The product SENSIPAR™ (cinacalcet hydrochloride) has been subject to a regulatory review period before its commercial marketing or use (35 U.S.C. 156(a)(4));
- (vi) The product, SENSIPAR™ (cinacalcet hydrochloride), has received permission for commercial marketing or use, and the permission for the commercial marketing or use of the product after the regulatory review period is the first permitted commercial marketing or use of the product under the provision of the Federal Food, Drug and Cosmetic Act, under which the regulatory review period occurred (35 U.S.C. 156(a)(5)(A));
- (vii) No other patent has been extended for the same regulatory review period for the product SENSIPAR™ (cinacalcet hydrochloride) (35 U.S.C. 156(c)(4)); and
- (viii) The owners of record of U.S. Patent No. 6,011,068 have hereby submitted an application to the Commissioner to obtain an extension of the term of the patent within the sixty (60) day period beginning on the date the product received permission for commercial marketing or use (35 U.S.C. 156(d)(1)).

12(B). The length of extension of the patent term of U.S. Patent No. 6,011,068 claimed by Applicants is 449 days. The length of extension was determined by the following:

- (i) The U.S. Patent No. 6,011,068 issued January 4, 2000, which was after the date of enactment of 35 U.S.C. 156. An exemption under §505(i) and an application under §505(b) were submitted with respect to the approved product after the date of enactment of 35 U.S.C. 156. The commercial marketing or use of the product, SENSIPAR™ (cinacalcet hydrochloride), was approved after the date of enactment of 35 U.S.C. 156.

- (ii) The regulatory review period under 35 U.S.C. 156(g)(1)(B) was from June 19, 1998, until March 8, 2004, which was 2089 days.
- (iii) The period of review under 35 U.S.C. 156(g)(1)(B)(i) began on the date an exemption under §505(i) became effective on June 19, 1998 and ended on the date an application was initially submitted for SENSIPAR™ (cinacalcet hydrochloride) under §505 which was September 5, 2003, a total of 1904 days.
- (iv) The regulatory review period under 35 U.S.C. 156(g)(1)(B)(ii) began on the date the application was initially submitted for the approved human drug product, SENSIPAR™ (cinacalcet hydrochloride), under §505(b), which was September 5, 2003 and ended on the date such application was approved under such section, which was March 8, 2004, a total of 185 days.
- (v) The issuance of U.S. Patent No. 6,011,068 occurred on January 4, 2000, which was 564 days after the effective date of the IND application (June 19, 1998).
- (vi) In compliance with §1.775(d)(1)(i), the number of days in the period set forth in item (v) of this paragraph 12(B) are subtracted from the period determined under 35 U.S.C. 156(g)(1)(B)(i), which is set forth in item (iii) of this paragraph 12(B), i.e., 1904 days, to provide an adjusted regulatory period under 35 U.S.C. 156(g)(1)(B)(i) of 1340 days.
- (vii) Under 35 U.S.C. 156(c)(2), the period of extension includes only one-half of the period determined under 35 U.S.C. 156(g)(1)(B)(i), which is set forth in item (vi) of this paragraph 12(B), which is 670 days, together the number of days required for approval set forth in item (iv) of this paragraph 12(B), i.e., 185 days, for an extension of 855 days.
- (viii) In compliance with 35 U.S.C. 156(c)(3), the period remaining in the term of U.S. Patent No. 6,011,068 after NDA approval of SENSIPAR™ (cinacalcet hydrochloride) is from March 8, 2004 to December 14, 2016 or 12.77 years, which when added to the period of extension under item (vii) of this paragraph 12(B), i.e., 855 days, is a total of 15.1 years, which is in excess of fourteen (14) years provided in 35 U.S.C. 156(c)(3). Therefore, the period of extension claimed by Applicant is 449 days for a total of 14 years after the date of NDA approval of SENSIPAR™ (cinacalcet hydrochloride), i.e., an expiration date of March 8, 2018.

13. Applicants acknowledge a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services any information which is material to the Determination of entitlement to the extension sought in this application.

14. The prescribed fee for receiving and acting upon the application for extension of \$1,120 is enclosed with this application. Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees. Should a refund of fee paid be necessary, the Commissioner is hereby authorized to credit any such amount to Deposit Account No. 19-0741.

15. Inquiries and correspondence relating to this application for patent term extension are to be directed to:

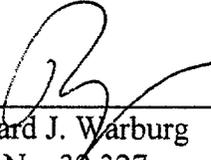
Richard J. Warburg, Esq.  
FOLEY & LARDNER, LLP  
P.O. Box 80278  
San Diego, CA 9213-0278  
TEL: (858) 847-6700  
FAX (858) 792-6773

16. Two additional copies of the application papers for extension of the patent term of US Patent No. 6,011,068 are enclosed with the application.

Respectfully submitted,

NPS Pharmaceuticals Inc. and Brigham & Women's Hospital

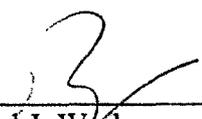
By

  
Richard J. Warburg  
Reg. No. 32,327

CERTIFICATION

The undersigned hereby certifies that this application for extension of patent term under 35 U.S.C. 156, including its attachments and supporting papers, is being submitted with two additional copies of originals.

Date 5/6/04

  
\_\_\_\_\_  
Richard J. Warburg  
Reg. No. 32,327

ATTACHMENT A  
COPY OF US PATENT NO. 6,011,068