

## Annex A

### Proposed Amended Claims to EP 0 817 637 B1

1. A combination consisting of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol or a physiologically functional derivative thereof and (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one or a physiologically functional derivative thereof.
- 4.2. A combination comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol or a physiologically functional derivative thereof and (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one or a physiologically functional derivative thereof.
- 2.3. A combination as claimed in claim 1 or 2 wherein the physiologically functional derivative of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol or (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one is a physiologically acceptable salt, ether, ester, salt of such ester, or solvate thereof.
- 3.4. A combination according to claim 24 comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol or a physiologically functional derivative thereof, zidovudine or a physiologically functional derivative thereof, and (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one or a physiologically functional derivative thereof.
- 4.5. A combination according to claim 43 wherein the physiologically functional derivative of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, zidovudine, or (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one is a physiologically acceptable salt, ether, ester, salt of such ester, or solvate thereof.
- 5.6. A combination according to claim 43 or 54 wherein the ratio of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol:zidovudine: (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one is in the ratio of 1 to 20: 1 to 20: 1 to 10 by weight.
- 6.7. A combination according to any claim from 1 to 65 for use in medical therapy.
- 7.8. A pharmaceutical formulation comprising a combination according to claims 1 to 65 in association with one or more pharmaceutically acceptable carriers therefor.
- 8.9. A formulation according to claim 87 in unit dosage form.
- 9.10. Use of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol and (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the manufacture of a medicament for the treatment and/or prophylaxis of an HIV infection.
- 10.11. Use of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, zidovudine and (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the manufacture of a medicament for the treatment and/or prophylaxis of an HIV infection.

- | 41.12. Use as claimed in claim 109 or 110 for the treatment and for prophylaxis of an HIV infection resistant to nucleoside or non-nucleoside inhibitors
- | 42.13. Use as claimed in claim 109 or 110 in the treatment of AIDS.
- | 43.14. Use as claimed in claim 109 or 110 in the treatment of AIDS related conditions or AIDS dementia complex.
- | 15. A product consisting of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a combined preparation for simultaneous, separate or sequential use in the treatment and/or prophylaxis of an HIV infection.
- | 44.16. A product comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a combined preparation for simultaneous, separate or sequential use in the treatment and/or prophylaxis of an HIV infection.
- | 45.17. A product comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, zidovudine and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a combined preparation for simultaneous, separate or sequential use in the treatment and/or prophylaxis of an HIV infection.
- | 46.18. A product as claimed in claim 175 wherein the components are present in the ratio of 1 to 20 : 1 to 20 : 1 to 10 by weight respectively.
- | 47.19. A product comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol as a preparation for simultaneous, separate or sequential use together with (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the treatment and/or prophylaxis of an HIV infection.
- | 48.20. A product comprising (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a preparation for simultaneous, separate or sequential use together with (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol in the treatment and/or prophylaxis of an HIV infection.
- | 49.21. A product comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol as a preparation for simultaneous, separate or sequential use together with zidovudine and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the treatment and/or prophylaxis of an HIV infection.
- | 20.22. A product comprising zidovudine as a preparation for simultaneous, separate or sequential use together with (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the treatment and/or prophylaxis of an HIV infection.
- | 24.23. A product comprising (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a preparation for simultaneous, separate or sequential use together with zidovudine and (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol in the treatment and/or prophylaxis of an HIV infection.

- | 22-24. A product comprising zidovudine and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a preparation for simultaneous, separate or sequential use together with (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol in the treatment and/or prophylaxis of an HIV infection.

## Annex B

### Proposed Amended Claims to EP 0 817 637 B1

1. A combination comprising two compounds selected from zidovudine or a physiologically functional derivative thereof, (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol or a physiologically functional derivative thereof and (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one or a physiologically functional derivative thereof provided that the two compounds are not zidovudine or a physiologically functional derivative thereof and (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one or a physiologically functional derivative thereof.
- 23.2. A combination comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol or a physiologically functional derivative thereof and (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one or a physiologically functional derivative thereof.
- 24.3. A combination as claimed in claim 1 or 2 wherein the physiologically functional derivative of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol or (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one is a physiologically acceptable salt, ether, ester, salt of such ester, or solvate thereof.
- 25.4. A combination according to claim 24 comprising (1 S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol or a physiologically functional derivative thereof, zidovudine or a physiologically functional derivative thereof, and (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one or a physiologically functional derivative thereof.
- 26.5. A combination according to claim 43 wherein the physiologically functional derivative of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, zidovudine, or (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one is a physiologically acceptable salt, ether, ester, salt of such ester, or solvate thereof.
- 27.6. A combination according to claim 3 or 4 or 5 wherein the ratio of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol:zidovudine: (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one is in the ratio of 1 to 20: 1 to 20: 1 to 10 by weight.
- 28.7. A combination according to any claim from 1 to 65 for use in medical therapy.
- 29.8. A pharmaceutical formulation comprising a combination according to claims 1 to 65 in association with one or more pharmaceutically acceptable carriers therefor.
- 30.9. A formulation according to claim 87 in unit dosage form.
- 31.10. Use of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the manufacture of a medicament for the treatment and/or prophylaxis of an HIV infection.

- | 32.11. Use of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, zidovudine and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the manufacture of a medicament for the treatment and/or prophylaxis of an HIV infection.
- | 33.12. Use as claimed in claim 109 or 110 for the treatment and for prophylaxis of an HIV infection resistant to nucleoside or non-nucleoside inhibitors
- | 34.13. Use as claimed in claim 109 or 110 in the treatment of AIDS.
- | 14. Use as claimed in claim 109 or 110 in the treatment of AIDS related conditions or AIDS dementia complex.
- | 35.15. A product comprising two compounds selected from zidovudine, (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one provided that the two compounds are not zidovudine and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a combined preparation for simultaneous, separate or sequential use in the treatment and/or prophylaxis of an HIV infection.
- | 36.16. A product comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a combined preparation for simultaneous, separate or sequential use in the treatment and/or prophylaxis of an HIV infection.
- | 37.17. A product comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, zidovudine and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a combined preparation for simultaneous, separate or sequential use in the treatment and/or prophylaxis of an HIV infection.
- | 38.18. A product as claimed in claim 175 wherein the components are present in the ratio of 1 to 20 : 1 to 20 : 1 to 10 by weight respectively.
- | 39.19. A product comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol as a preparation for simultaneous, separate or sequential use together with (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the treatment and/or prophylaxis of an HIV infection.
- | 40.20. A product comprising (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a preparation for simultaneous, separate or sequential use together with (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol in the treatment and/or prophylaxis of an HIV infection.
- | 41.21. A product comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol as a preparation for simultaneous, separate or sequential use together with zidovudine and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the treatment and/or prophylaxis of an HIV infection.
- | 42.22. A product comprising zidovudine as a preparation for simultaneous, separate or sequential use together with (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the treatment and/or prophylaxis of an HIV infection.

- | 43:23. A product comprising (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a preparation for simultaneous, separate or sequential use together with zidovudine and (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol in the treatment and/or prophylaxis of an HIV infection.
- | 24. A product comprising zidovudine and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a preparation for simultaneous, separate or sequential use together with (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol in the treatment and/or prophylaxis of an HIV infection.