[0003] Today only three drugs have been approved for use against RSV infection. A first one is ribavirin, a nucleoside analogue that provides an aerosol treatment for serious RSV infection in hospitalized children. The other two drugs, RespiGam® (RSV-IG) and Synagis® (palivizumab), polyclonal and monoclonal antibody immunostimulants, are intended to be used in a preventive way. Both are very expensive, and require parenteral administration. A number of compounds are in clinical development for the treatment of RSV infection. One of those compounds is 3-({5-chloro-1-[3-(methylsulfonyl)-propyl]-1*H*-indol-2-yl}methyl)-1-(2,2,2-trifluoroethyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one disclosed in WO-2012/080447 as compound P55.

[0004] It has now been found that the combination of 3-({5-chloro-1-[3-(methylsulfonyl)-propyl]-1*H*-indol-2-yl}methyl)-1-(2,2,2-trifluoroethyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one (hereinafter referred to as Compound A) and one or more Compound B, wherein Compound B has RSV replication inhibiting properties, provides an improved therapy in the treatment of RSV infection.

[0005] Some embodiments disclosed herein relate to the combination of Compound A and one or more Compound B and the use of this combination for treating or ameliorating RSV infection in a subject in need thereof.

[0006] Other embodiments relate to a pharmaceutical product comprising the combination of Compound A and one or more Compound B and the use of said pharmaceutical product for treating or ameliorating RSV infection.

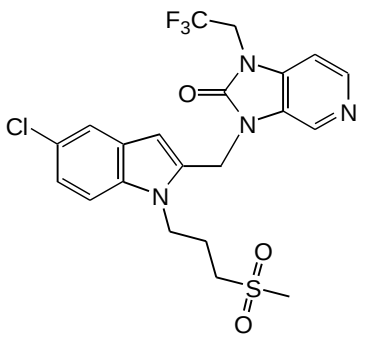
[0006a] In one aspect, the present disclosure relates to a pharmaceutical composition comprising a combination comprising 3-({5-chloro-1-[3-(methylsulfonyl)propyl]-1H-indol-2-yl}methyl)-1-(2,2,2-trifluoroethyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, or a pharmaceutically acceptable salt thereof, as Compound A, and one or more Compound B selected from ribavirin, GS 5806, MDT 637, A 60444, AZ-27, CR9501, palivizumab, N-(2-fluoro-6-methylphenyl)-6-(4-(5-methyl-2-(7-oxa-2-azaspiro[3.5]nonan-2-yl)nicotinamido)-benzoyl)-5,6-dihydro-4H-benzo[b]thieno[2,3-d]azepine-2-carboxamide, and 4-amino-8-[3-[[2-(3,4-dimethoxyphenyl)ethyl]amino]propyl]-6,6-dimethyl-2-(4-methyl-3-nitrophenyl)-3H-imidazo[4,5-h]isoquinoline-7,9(6H,8H)-dione, or a pharmaceutically acceptable salt thereof; and a pharmaceutically acceptable carrier.

[0007] Still other embodiments relate to a method of treating or ameliorating RSV infection in a subject in need thereof comprising administering the combination of Compound A and one or more Compound B in an effective amount to said subject.

[0007a] In another aspect, the present disclosure relates to use of a combination as defined herein in the manufacture of a medicament for the treatment or amelioration of RSV infection.

[0007b] In another aspect, the present disclosure relates to use of a pharmaceutical composition as defined herein in the manufacture of a medicament for the treatment or amelioration of RSV infection.

[0008] Compound A is 3-({5-chloro-1-[3-(methylsulfonyl)propyl]-1*H*-indol-2-yl}methyl)-1-(2,2,2-trifluoroethyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one disclosed in WO-2012/080447 as compound P55 having the following structure :



Claims

1. A pharmaceutical composition comprising a combination comprising 3-({5-chloro-1-[3-(methylsulfonyl)propyl]-1*H*-indol-2-yl}methyl)-1-(2,2,2-trifluoroethyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, or a pharmaceutically acceptable salt thereof, as Compound A, and
one or more Compound B selected from ribavirin, GS-5806, MDT-637, A-60444, AZ-27, CR9501, palivizumab, N-(2-fluoro-6-methylphenyl)-6-(4-(5-methyl-2-(7-oxa-2-azaspiro[3.5]nonan-2-yl)nicotinamido)-benzoyl)-5,6-dihydro-4H-benzo[b]thieno[2,3-d]azepine-2-carboxamide, and 4-amino-8-[3-[[2-(3,4-dimethoxyphenyl)ethyl]amino] propyl]-6,6-dimethyl-2-(4-methyl-3-nitrophenyl)-3H-imidazo[4,5-h]isoquinoline-7,9(6H, 8H)-dione, or a pharmaceutically acceptable salt thereof;
and a pharmaceutically acceptable carrier.

2. The pharmaceutical composition according to claim 1 wherein Compound B is ribavirin.

3. The pharmaceutical composition according to claim 1 wherein Compound B is GS-5806.

4. The pharmaceutical composition according to claim 1 wherein Compound B is MDT-637.

5. The pharmaceutical composition according to claim 1 wherein Compound B is A-60444.

6. The pharmaceutical composition according to claim 1 wherein Compound B is a monoclonal antibody selected from CR9501, and palivizumab.

7. The pharmaceutical composition according to claim 1 wherein Compound B is N-(2-fluoro-6-methylphenyl)-6-(4-(5-methyl-2-(7-oxa-2-azaspiro[3.5]nonan-2-yl)nicotinamido) benzoyl)-5,6-dihydro-4H-benzo[b]thieno[2,3-d]azepine-2-carboxamide.

8. The pharmaceutical composition according to claim 1 wherein Compound B is 4-amino-8-[3-[[2-(3,4-dimethoxyphenyl)ethyl]amino]propyl]-6,6-dimethyl-2-(4-methyl-3-nitrophenyl)-3H-imidazo[4,5-h]isoquinoline-7,9(6H,8H)-dione.

9. The pharmaceutical composition according to any one of claims 1 to 8 wherein the amount of Compound A and the amount of Compound B is such that a synergistic antiviral effect against RSV is obtained.

10. The pharmaceutical composition according to claim 9 wherein the amount of Compound A ranges from 10 mg to 2500 mg and the amount of Compound B ranges from 10 mg to 2500 mg.

11. Use of a combination as defined in any one of claims 1 to 10 in the manufacture of a medicament for the treatment or amelioration of RSV infection.

12. Use of a pharmaceutical composition according to any one of claims 1 to 10 in the manufacture of a medicament for the treatment or amelioration of RSV infection.