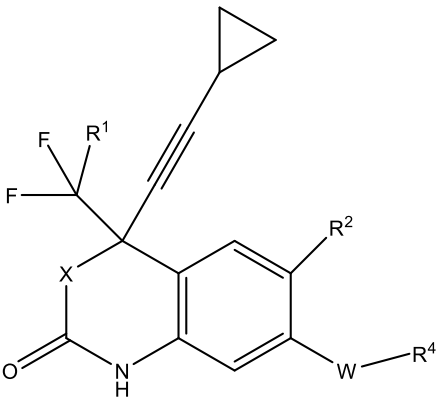
non-infectious. Once integration has occurred, a cell is infected until it dies through either normal cell death pathways, accelerated death due to viral factors, or is targeted by the immune system. While most infected cells are expected to die within ~2 days of being infected, the rapid rebound of viremia when therapy is removed is an indication that infected cells remain even after years on therapy (*See*, e.g., J. B. Dinoso *et al*., Proc. Natl. Acad. Sci. U.S.A., 2009, 106(23): 9403-9408). These latently infected and/or persistently virus-expressing cells that remain even during antiretroviral therapy are collectively termed the HIV reservoir and are the reason that people living with HIV require life-long treatment with a high level of adherence to maintain virus at undetectable levels. Thus, new therapies that can selectively kill the HIV infected cells would provide new treatment options for HIV infection. These targeted activator of cell kill (TACK) molecules bind the reverse transcriptase-p66 domain of monomeric Gag-Pol and act as allosteric modulators to accelerate dimerization, resulting in HIV-$1^+$ cell death through premature intracellular viral protease activation. TACK molecules retain potent antiviral activity and selectively eliminate infected $CD4^+$ T cells isolated from people living with HIV-1, thus supporting an immune-independent clearance strategy (*See*, e.g., C. J. Balibar, *et al*., Sci. Transl. Med., 2023, 684 (15):eabn2038)

**[0005]** Treatment with compounds that can accelerate death of HIV infected cells and decrease the overall number of virally infected cells that persist within patients has the potential to decrease residual viremia in HIV suppressed individuals and address co-morbidities associated with chronic viral infection such as chronic inflammation, immune dysfunction, accelerated aging, cardiovascular disease (CVD), central nervous system (CNS) and other tissue and end-organ damage. Furthermore, treatment with compounds that can purge the remaining HIV reservoir may prolong viral remission off therapy and play a role in an HIV cure strategy.

## SUMMARY

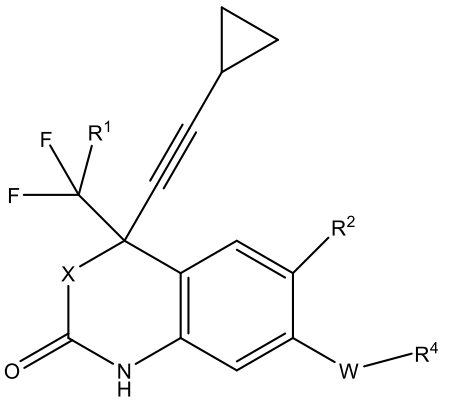
**[0006]** The present disclosure is directed to tetrahydroquinazoline derivatives and their use as HIV-Targeted Activator of Cell Kill agents which accelerate the death of HIV GAG-POL expressing cells without concomitant cytotoxicity to HIV naïve cells. Accordingly, the compounds are useful for selectively killing HIV infected, GAG-POL expressing cells in a subject infected with HIV. Additionally, the compounds disclosed herein are useful for the treatment or prophylaxis of infection by HIV, or for the treatment, prophylaxis or delay in the onset or progression of AIDS or AIDS Related Complex (ARC). Compositions and methods of use comprising the compounds of this disclosure are also provided.

**[0007]** The present disclosure provides compounds of Formula (I)



(**I**), and their pharmaceutically acceptable salts.

**[0007a]** In one aspect, the present disclosure provides a compound of Formula I:



(**I**)

or a pharmaceutically acceptable salt thereof, wherein:

**X** is N(**R3**) or C(**R3**);

**W** is -$C_{1-6}$ alkyl-, -($C_{0-6}$ alkyl)O-, -($C_{1-6}$ alkyl)amino-, or -($C_{1-6}$ alkyl)aminocarbonyl-,

wherein W is substituted by 0, 1, or 2 **R5** substituents;

each **R5** independently is halo, $C_{1-4}$ alkyl or $C_{1-4}$ fluoroalkyl;

**R1** is halo, $C_{1-6}$ alkyl, ($C_{3-12}$)heterocycloalkyl($C_{0-4}$ alkyl), or ($C_{3-12}$)cycloalkyl($C_{0-4}$ alkyl);

**R2** is hydrogen, halo, or $C_{1-10}$ alkyl;

**R3** is hydrogen, halo, or $C_{1-10}$ alkyl;

**R4** is selected from:

**a)** a 5-membered heteroaryl having at least one nitrogen atom,

**b)** a mono-, bicyclic- or tricyclic, 7- to 14-membered heteroaryl comprising at least one aromatic heteroatom containing ring, wherein said 7- to 14-member heteroaryl comprises at least one nitrogen atom, or

**c)** a ketone containing ring system selected from triazolinonyl, 2,4-dihydro-3*H*-1,2,4-triazoly-3-onyl, dihydropyrrolo[3, 4-*b*]pyrrolonyl, imidazolidinonyl, 1,3-dihydro-2H-benzo[d]imidazole-2-onyl, dihydrobenzo[d]imidazolinonyl, 1,3-dihydroimidazo[4,5-*c*]pyridinonyl, oxazolo[5,4-*c*]pyridine-2-onyl, 1,5,6,7-tetrahydro-pyrrolo[3,2-c]pyridin-4-onyl, 1,3-dihydroimidazo[4,5-*b*]pyridine-2-onyl, isoindolinonyl, 4,5-dihydropyrrolo[3,4-*b*]pyrrolonyl, 4,5-dihydropyrrolo[3,4-*b*]pyrrol-6(*2H*)onyl, benzo[*d*]oxazolonyl, benzo[*d*]oxazol-2-onyl, 1,4,5,6-tetrahydrocyclopenta[*c*]pyrazolonyl, and 1,5,6,7- tetrahydro-pyrazolo[4,3-*c*]pyridine-4-onyl;

wherein $\mathbf{R^4}$ is substituted by 0, 1, 2, or 3 $\mathbf{R^{4a}}$ substituents;

each $\mathbf{R^{4a}}$ independently is selected from:

$C_{1\text{-}6}$ alkyl,

$C_{1\text{-}10}$ fluoroalkyl,

amino,

cyano,

halo,

hydroxy,

($C_{1\text{-}10}$ alkyloxy)$C_{0\text{-}10}$ alkyl,

$C_{1\text{-}10}$ fluoroalkyloxy,

-($C_{1\text{-}10}$ alkyl)OH,

($C_{1\text{-}6}$ alkyl)$_{1\text{-}2}$ amino($C_{0\text{-}10}$ alkyl),

amino($C_{1\text{-}10}$ alkyl),

aminocarbonyl($C_{0\text{-}10}$ alkyl),

($C_{3\text{-}12}$)cycloalkyl($C_{0\text{-}6}$ alkyl),

($C_{5\text{-}6}$)heteroaryl($C_{0\text{-}6}$ alkyl),

($C_{6\text{-}14}$)aryl($C_{0\text{-}6}$ alkyl),

-($C_{0\text{-}4}$ alkyl)carbonyl, and

–($C_{0\text{-}5}$ alkyl)–($S(=O)_2NH_2$);

wherein $\mathbf{R^{4a}}$ is substituted by 0, 1, 2, or 3 $\mathbf{R^{4b}}$ substituents; and

each $\mathbf{R^{4b}}$ independently is $C_{1\text{-}10}$ alkyloxy, $C_{1\text{-}6}$ alkyl, $C_{1\text{-}10}$ fluoroalkyl, amino, hydroxy, halo, or cyano.

**[0007b]** In another aspect, the present disclosure provides a pharmaceutical composition comprising an effective amount of the compound as defined herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

**[0007c]** In another aspect, the present disclosure provides use of the compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of infection by HIV, or for the treatment, prophylaxis or delay in the onset or progression of AIDS or ARC.

**[0007d]** In another aspect, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, for use in eliciting GAG-POL dimerization in HIV-infected cells in a human subject in need thereof.

**[0007e]** In another aspect, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, for use in selectively killing HIV infected GAG-POL expressing cells in a human subject.

**[0007f]** In another aspect, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, for use in selectively killing HIV infected GAG-POL expressing cells without concomitant cytotoxicity to HIV naïve cells in a human subject.

**[0007g]** In another aspect, the present disclosure provides a compound as defined herein, or a pharmaceutically acceptable salt thereof, for use in augmenting the suppression of HIV viremia in a human subject whose viremia is being suppressed by administration of one or more compatible HIV antiviral agents.

**[0007h]** In another aspect, the present disclosure provides the compound as defined herein for use in therapy.

## DETAILED DESCRIPTION OF THE INVENTION

**[0008]** The present disclosure is directed to tetrahydroquinazoline derivative compounds and their use for accelerating the death of HIV GAG-POL expressing cells without concomitant cytotoxicity to HIV naïve cells. In the absence of compounds such as those from the present disclosure, protease (PR) activation takes place during viral maturation and the concentration of mature PR in the cytoplasm is limited. In contrast, the present compounds promote the desired phenotype by catalyzing GAG-POL dimerization inside the infected cell by binding to the immature RT binding site and triggering premature activation of the HIV PR enzyme inside the host infected cell prior to budding. As a result, PR cleaves host substrates within the cell, leading

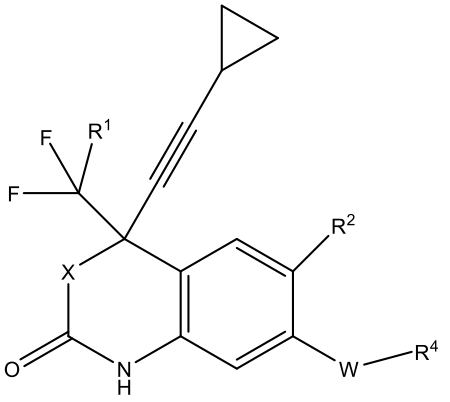
to cytotoxicity and cell death. This effect can be blocked in the presence of an HIV protease inhibitor such as indinavir or darunavir demonstrating the role of HIV protease in the process.

**[0009]** The compounds presently disclosed herein also have activity as Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs), due to the homology between the mature and immature RT pocket in HIV that allows the compounds to bind to the mature hydrophobic pocket near the active site of the viral RT enzyme. Binding to mature RT results in inhibition of enzymatic activity and production of the DNA provirus, which prevents infection of naïve CD4+ T-cells.

**[0010]** While effects of NNRTIs on dimerization of RT and GAG-POL have been documented (Tachedjian et al. Proc. Natl. Acad. Sci. U.S.A. 2001, 98(13):7188; Tachedjian et al. FEBS Lett. 2005, 579:379; Figueiredo et al. PLOS Path. 2006, 2(11):1051; Sudo et al. J. Virol. 2013, 87(6):3348), selective killing of HIV infected cells as a result of enhanced dimerization was first reported by Jochmans et al. (Jochmans et al. Retrovirology 2010, 7:89). The authors generated data showing these effects in chronically infected MT-4 cells, PBMCs, and CD4+ cells. Based on

WHAT IS CLAIMED IS:

1. A compound of Formula I:




(**I**)

or a pharmaceutically acceptable salt thereof, wherein:

**X** is N(**R3**) or C(**R3**);

**W** is -$C_{1-6}$ alkyl-, -($C_{0-6}$ alkyl)O-, -($C_{1-6}$ alkyl)amino-, or -($C_{1-6}$ alkyl)aminocarbonyl-,

wherein W is substituted by 0, 1, or 2 **R5** substituents;

each **R5** independently is halo, $C_{1-4}$ alkyl or $C_{1-4}$ fluoroalkyl;

**R1** is halo, $C_{1-6}$ alkyl, ($C_{3-12}$)heterocycloalkyl($C_{0-4}$ alkyl), or ($C_{3-12}$)cycloalkyl($C_{0-4}$ alkyl);

**R2** is hydrogen, halo, or $C_{1-10}$ alkyl;

**R3** is hydrogen, halo, or $C_{1-10}$ alkyl;

**R4** is selected from:

**a)** a 5-membered heteroaryl having at least one nitrogen atom,

**b)** a mono-, bicyclic- or tricyclic, 7- to 14-membered heteroaryl comprising at least one aromatic heteroatom containing ring, wherein said 7- to 14-member heteroaryl comprises at least one nitrogen atom, or

**c)** a ketone containing ring system selected from triazolinonyl, 2,4-dihydro-3*H*-1,2,4-triazoly-3-onyl, dihydropyrrolo[3, 4-*b*]pyrrolonyl, imidazolidinonyl, 1,3-dihydro-2H-benzo[d]imidazole-2-onyl, dihydrobenzo[d]imidazolinonyl, 1,3-dihydroimidazo[4,5-*c*]pyridinonyl, oxazolo[5,4-*c*]pyridine-2-onyl, 1,5,6,7-tetrahydro-pyrrolo[3,2-c]pyridin-4-onyl, 1,3-dihydroimidazo[4,5-*b*]pyridine-2-onyl, isoindolinonyl, 4,5-dihydropyrrolo[3,4-*b*]pyrrolonyl, 4,5-dihydropyrrolo[3,4-*b*]pyrrol-6(*2H*)onyl, benzo[*d*]oxazolonyl, benzo[*d*]oxazol-2-onyl, 1,4,5,6-

tetrahydrocyclopenta[*c*]pyrazolonyl, and 1,5,6,7- tetrahydro-pyrazolo[4,3-*c*]pyridine-4-onyl;

wherein $\mathbf{R^4}$ is substituted by 0, 1, 2, or 3 $\mathbf{R^{4a}}$ substituents;

each $\mathbf{R^{4a}}$ independently is selected from:

$C_{1\text{-}6}$ alkyl,

$C_{1\text{-}10}$ fluoroalkyl,

amino,

cyano,

halo,

hydroxy,

($C_{1\text{-}10}$ alkyloxy)$C_{0\text{-}10}$ alkyl,

$C_{1\text{-}10}$ fluoroalkyloxy,

-($C_{1\text{-}10}$ alkyl)OH,

($C_{1\text{-}6}$ alkyl)$_{1\text{-}2}$ amino($C_{0\text{-}10}$ alkyl),

amino($C_{1\text{-}10}$ alkyl),

aminocarbonyl($C_{0\text{-}10}$ alkyl),

($C_{3\text{-}12}$)cycloalkyl($C_{0\text{-}6}$ alkyl),

($C_{5\text{-}6}$)heteroaryl($C_{0\text{-}6}$ alkyl),

($C_{6\text{-}14}$)aryl($C_{0\text{-}6}$ alkyl),

-($C_{0\text{-}4}$ alkyl)carbonyl, and

–($C_{0\text{-}5}$ alkyl)–(S(=O)$_2$NH$_2$);

wherein $\mathbf{R^{4a}}$ is substituted by 0, 1, 2, or 3 $\mathbf{R^{4b}}$ substituents; and

each $\mathbf{R^{4b}}$ independently is $C_{1\text{-}10}$ alkyloxy, $C_{1\text{-}6}$ alkyl, $C_{1\text{-}10}$ fluoroalkyl, amino, hydroxy, halo, or cyano.

2. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein **X** is N($\mathbf{R^3}$).

3. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein **X** is C($\mathbf{R^3}$).

4. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein **W** is -$C_{1-6}$ alkyl-, -($C_{1-6}$ alkyl)amino-, or -($C_{1-6}$ alkyl)aminocarbonyl, wherein W is substituted by 0, 1, or 2 $\mathbf{R^5}$ substituents.

5. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein **W** is -($C_{0-6}$ alkyl)O-, wherein W is substituted by 0, 1, or 2 $\mathbf{R^5}$ substituents.

6. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein $\mathbf{R^1}$ is fluoro, chloro, bromo, methyl, ethyl, *n*-propyl, isopropyl, butyl, isobutyl, *sec*-butyl, *tert*-butyl, pentyl, isopentyl, neopentyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclopropylmethyl, cyclobutylmetyl, cyclopentylmethyl, or cyclohexylmethyl.

7. The compound of claim 6 or a pharmaceutically acceptable salt thereof, wherein $\mathbf{R^2}$ is hydrogen, fluoro, chloro, bromo, methyl, ethyl, *n*-propyl, isopropyl, butyl, isobutyl, *sec*-butyl, *tert*-butyl, pentyl, isopentyl, or neopentyl.

8. The compound of claim 7 or a pharmaceutically acceptable salt thereof, $\mathbf{R^3}$ is hydrogen, fluoro chloro, methyl, bromo, ethyl, *n*-propyl, isopropyl, butyl, isobutyl, *sec*-butyl, *tert*-butyl, pentyl, isopentyl, or neopentyl.

9. The compound of any one of claims 1 to 8 or a pharmaceutically acceptable salt thereof wherein $\mathbf{R^4}$ is selected from:

**a)** a 5-membered heteroaryl having at least one nitrogen atom, the 5-membered heteroaryl having at least one nitrogen atom, is selected from: triazolyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, pyrrolyl, tetrazolyl, furazanyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, and 1,2,3,5-oxatriazolyl;

**b)** a mono-, bicyclic- or tricyclic, 7- to 14-membered heteroaryl comprising at least one aromatic heteroatom containing ring, wherein said 7- to 14-member heteroaryl comprises at least one nitrogen atom, and the mono-, bicyclic- or tricyclic, 7- to 14-membered heteroaryl comprising at least one aromatic heteroatom containing ring,

wherein said 7- to 14-member heteroaryl comprises at least one nitrogen atom is selected from 2*H*-pyrazolo [4,3-*c*]pyridinyl, 1*H*-pyrazolo[3,4-*c*]pyridinyl, 6,7-dihydropyrano[4,3-c]pyrazolyl, 2*H*-pyrazolo[3,4-*d*]pyrimidinyl, 2*H*-pyrazolo[3,4-*d*]pyrimidinyl, indolyl, 2*H*-pyrazolo[3,4-*b*]pyridinyl, benzo[*d*][1,2,3]-triazolyl, benzo[*d*]imidazolyl, indolizinyl, isoindolyl, purinyl, quinolizinyl, isoquinolyl, quinolyl, phthalazinyl, naphthyridinyl, quinoxalinyl, cinnolinyl, carbazolyl, phenathridinyl, acridinyl, phenanthrolinyl, phenazinyl, 7H-pyrazino[2,3-c]carbazolyl, 1,3-benzooxazolyl, and 2,1-benzoxazolyl, or

**c)** a ketone containing ring system selected from the ketone containing ring system selected from 2,4-dihydro-3*H*-1,2,4-triazoly-3-onyl, imidazolidinonyl, 1,3-dihydro-2H-benzo[d]imidazole-2-onyl, 1,3-dihydroimidazo[4,5-*c*]pyridinonyl, isoindolinonyl, 4,5-dihydropyrrolo[3,4-*b*]pyrrol-6(*2H*)onyl, and benzo[*d*]oxazol-2onyl, 1,4,5,6-tetrahydrocyclopenta[*c*]pyrazolonyl, and

further wherein $\mathbf{R^4}$ is substituted by 0, 1, 2, or 3 $\mathbf{R^{4a}}$ substituents.

10. The compound of claim 9 or a pharmaceutically acceptable salt thereof wherein each $\mathbf{R^{4a}}$ independently is selected from: $C_{1\text{-}4}$ alkyl, $C_{1\text{-}6}$ fluoroalkyl, amino, cyano, halo, hydroxy, ($C_{1\text{-}6}$ alkyloxy)$C_{0\text{-}6}$ alkyl, $C_{1\text{-}6}$ fluoroalkyloxy, -($C_{1\text{-}6}$ alkyl)OH, ($C_{1\text{-}4}$ alkyl)$_{1\text{-}2}$ amino($C_{0\text{-}6}$ alkyl), amino($C_{1\text{-}6}$ alkyl), aminocarbonyl($C_{0\text{-}6}$)alkyl), ($C_{3\text{-}12}$)cycloalkyl($C_{0\text{-}4}$ alkyl), ($C_{5\text{-}6}$)heteroaryl($C_{0\text{-}4}$ alkyl), ($C_{6\text{-}14}$)aryl($C_{0\text{-}6}$ alkyl), -($C_{0\text{-}4}$ alkyl)carbonyl, and –($C_{0\text{-}4}$ alkyl)–($S(=O)_2NH_2$), wherein $\mathbf{R^{4a}}$ is substituted by 0, 1, 2, or 3 $\mathbf{R^{4b}}$ substituents.

11. The compound of claim 10 or a pharmaceutically acceptable salt thereof wherein each $\mathbf{R^{4b}}$ independently is selected from $C_{1\text{-}6}$ alkyloxy, $C_{1\text{-}4}$ alkyl, $C_{1\text{-}6}$ fluoroalkyl, amino, hydroxy, halo, or cyano.

12. The compound of claim 11 or a pharmaceutically acceptable salt thereof wherein each $\mathbf{R^5}$ independently is fluoro, chloro, methyl, ethyl, propyl, trifluoromethyl, 2,2,2-trifluoroethyl, difluoromethyl, or fluoromethyl.

13. The compound of claim 1 that is:

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-methoxy-1*H*-1,2,4-triazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-(hydroxymethyl)-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((4-methoxy-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-(hydroxymethyl)-1*H*-1,2,4-triazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-6-fluoro-7-((5-(hydroxymethyl)-1*H*-pyrazol-1-yl)methyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-6-fluoro-7-((3-(hydroxymethyl)-1*H*-pyrazol-1-yl)methyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-6-fluoro-7-((2-oxo-1,2-dihydro-3*H*-imidazo[4,5-*b*]pyridin-3-yl)methyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-7-((2-oxo-2,3-dihydro-1*H*-imidazo[4,5-*b*]pyridin-1-yl)methyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-3-((4-(cyclopropylethynyl)-6-fluoro-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1-methylimidazolidine-2,4-dione;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((4-(pyridin-4-yl)-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((4-methyl-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-3-((4-(cyclopropylethynyl)-6-fluoro-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)benzo[d]oxazol-2(3*H*)-one;

(*S*)-3-((4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-2-oxo-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)imidazolidine-2,4-dione;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((4-fluoro-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((4-chloro-1*H*-pyrazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-1-((4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-2-oxo-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1*H*-pyrazole-3-carbonitrile;

(*S*)-7-((5-chloro-3-(methoxymethyl)-1*H*-pyrazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((3-bromo-1*H*-pyrazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((1*H*-1,2,4-triazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((2*H*-pyrazolo[4,3-c]pyridin-2-yl)methyl)-4-(cyclopropylethynyl)-6-fluoro-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-7-((6,7-dihydropyrano[4,3-c]pyrazol-1(4*H*)-yl)methyl)-6-fluoro-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-7-((6,7-dihydropyrano[4,3-c]pyrazol-2(4*H*)-yl)methyl)-6-fluoro-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-6-fluoro-7-((2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)methyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-7-((1,3-dimethyl-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)methyl)-6-fluoro-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-6-fluoro-7-((3-methyl-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)methyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-6-fluoro-7-((5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)methyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((3-chloro-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((3-chloro-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)methyl)-4-(cyclopropylethynyl)-6-fluoro-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((3-cyclopropyl-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)methyl)-4-(cyclopropylethynyl)-6-fluoro-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-methyl-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-6-fluoro-7-((2-oxo-2,3-dihydro-1*H*-imidazo[4,5-*c*]pyridin-1-yl)methyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((6-oxo-5,6-dihydropyrrolo[3,4-b]pyrrol-1(4*H*)-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-6-fluoro-7-((2-oxo-1,2-dihydro-3*H*-imidazo[4,5-*c*]pyridin-3-yl)methyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-3-((4-(cyclopropylethynyl)-6-fluoro-3-methyl-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)imidazolidine-2,4-dione;

(*S*)-7-((3-amino-1*H*-pyrazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((3-amino-5-methyl-1*H*-pyrazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((3-amino-4-methyl-1*H*-pyrazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((3-amino-1*H*-pyrazol-1-yl)methyl)-4-(cyclopropyldifluoromethyl)-4-(cyclopropylethynyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-(2-hydroxyethyl)-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-6-chloro-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-7-((3-(hydroxymethyl)-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((2-(hydroxymethyl)-1*H*-imidazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((5-(hydroxymethyl)-1*H*-imidazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((4-(hydroxymethyl)-1*H*-imidazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-(1*H*,1'*H*-[3,3'-bipyrazol]-1-ylmethyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((1'-methyl-1*H*,1'*H*-[3,3'-bipyrazol]-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-(methoxymethyl)-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((1*H*-pyrazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((1*H*-imidazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-methoxy-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-((*R* or *S*)-1-methoxyethyl)-1H-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-((*S* or *R*)-1-methoxyethyl)-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((3-amino-5-chloro-1*H*-pyrazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-oxo-3,4,5,6-tetrahydrocyclopenta[c]pyrazol-1(2*H*)-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-1-((4-(cyclopropyldifluoromethyl)-4-(cyclopropylethynyl)-6-fluoro-2-oxo-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1*H*-imidazole-2-carboxamide;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-7-((3-(difluoromethoxy)-1*H*-pyrazol-1-yl)methyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((4-(methoxymethyl)-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-(methoxymethyl)-1*H*-1,2,4-triazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((4-chloro-3-(methoxymethyl)-1*H*-pyrazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((4-fluoro-3-(hydroxymethyl)-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-(hydroxymethyl)-4-methyl-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((5-chloro-3-(hydroxymethyl)-1*H*-pyrazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((4-(2-hydroxyethyl)-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(S)-7-((4-chloro-3-(hydroxymethyl)-1H-pyrazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1H)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-((*S* or *R*)-1-hydroxyethyl)-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-((*R* or *S*)-1-hydroxyethyl)-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((2-methoxy-1*H*-imidazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-(methylamino)-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-7-((3-(dimethylamino)-1*H*-pyrazol-1-yl)methyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-chloro-*N*-((4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-2-oxo-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1*H*-imidazole-5-carboxamide;

(*S*)-4-chloro-*N*-((4-(cyclopropylethynyl)-6-fluoro-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1*H*-imidazole-5-carboxamide;

(*S*)-*N*-((4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-2-oxo-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1*H*-imidazole-2-carboxamide;

(*S*)-*N*-((4-(cyclopropylethynyl)-6-fluoro-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1*H*-imidazole-2-carboxamide;

(*S*)-*N*-((4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-2-oxo-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-*N*-methyl-1*H*-imidazole-2-carboxamide;

(*S*)-*N*-((4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-2-oxo-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1-methyl-1*H*-imidazole-2-carboxamide;

(*S*)-*N*-((4-(cyclopropylethynyl)-6-fluoro-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)oxazole-2-carboxamide;

(*S*)-2-amino-*N*-((4-(cyclopropylethynyl)-6-fluoro-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-4-methylthiazole-5-carboxamide;

(*S*)-*N*-((4-(cyclopropylethynyl)-6-fluoro-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-4*H*-1,2,4-triazole-3-carboxamide;

(*S*)-*N*-((4-(cyclopropylethynyl)-6-fluoro-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-3-methyl-1*H*-pyrrole-2-carboxamide;

(*S*)-*N*-((4-(cyclopropylethynyl)-6-fluoro-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-4-methyl-1*H*-imidazole-5-carboxamide;

(*S*)-4-cyano-N-((4-(cyclopropylethynyl)-6-fluoro-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1*H*-pyrrole-2-carboxamide;

(*S*)-*N*-((4-(cyclopropylethynyl)-6-fluoro-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)thiazole-2-carboxamide;

(*S*)-7-((2*H*-indazol-2-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((1*H*-indazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((1*H*-benzo[d][1,2,3]triazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-methyl-1*H*-indazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((1*H*-benzo[d]imidazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((4-chloro-3-methoxy-1*H*-pyrazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-6-fluoro-7-((1-oxoisoindolin-2-yl)methyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-(4-methoxyphenyl)-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-6-fluoro-7-((4-oxo-4,5,6,7-tetrahydro-1*H*-pyrrolo[3,2-c]pyridin-1-yl)methyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

*(S)*-7-((3-amino-4-methoxy-1*H*-pyrazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-1-((4-(cyclopropylethynyl)-6-fluoro-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1*H*-imidazole-2-carboxamide;

(*S*)-4-(cyclopropylethynyl)-6-fluoro-7-((3-methyl-1*H*-pyrazol-1-yl)methyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-1-((4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-2-oxo-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1*H*-pyrazole-3-carbaldehyde;

(*S*)-1-((4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-2-oxo-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-4-fluoro-1*H*-pyrazole-5-carboxamide;

(*S*)-1-((4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-2-oxo-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-4-fluoro-1*H*-pyrazole-3-carboxamide;

(*S*)-7-((5-amino-1*H*-1,2,4-triazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((3-amino-1*H*-1,2,4-triazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((3-amino-1*H*-1,2,4-triazol-1-yl)methyl)-4-(cyclopropylethynyl)-6-fluoro-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-7-((1,3-dimethyl-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)methyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-3-((4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-2-oxo-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1-methylimidazolidine-2,4-dione;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((methyl(1*H*-pyrazol-3-yl)amino)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-(methoxymethyl)-1*H*-pyrazol-1-yl)methyl)-3-methyl-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-1-((4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-2-oxo-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1*H*-1,2,4-triazole-3-carboxamide;

(*S*)-1-((4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-2-oxo-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1*H*-1,2,4-triazole-5-carboxamide;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((4-fluoro-3-methoxy-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-1-((4-(cyclopropylethynyl)-6-fluoro-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1*H*-1,2,4-triazole-5-carboxamide;

(*S*)-1-((4-(cyclopropylethynyl)-6-fluoro-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1*H*-1,2,4-triazole-3-carboxamide;

(*S*)-4-(cyclopropylethynyl)-6-fluoro-7-((5-methyl-2*H*-tetrazol-2-yl)methyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((2*H*-indazol-3-yl)methyl)-4-(cyclopropylethynyl)-6-fluoro-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-1-((4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-2-oxo-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1*H*-pyrazole-3-sulfonamide;

(S)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-7-((4-(difluoromethyl)-1H-pyrazol-1-yl)methyl)-6-fluoro-3,4-dihydroquinazolin-2(1H)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((4-methyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-6-chloro-4-(cyclopropylethynyl)-7-((4-methoxy-1*H*-pyrazol-1-yl)methyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

5-(((*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-2-oxo-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1-methylimidazolidine-2,4-dione;

(*S*)-5-(((*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-2-oxo-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1-methylimidazolidine-2,4-dione;

(*R*)-5-(((*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-2-oxo-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1-methylimidazolidine-2,4-dione;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-7-((3-((dimethylamino)methyl)-1*H*-pyrazol-1-yl)methyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-7-((3-methyl-1H-pyrazol-1-yl)methyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-7-((3,4-dimethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-1-yl)methyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one; and

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-(2-hydroxypropan-2-yl)-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one,

or a pharmaceutically acceptable salt thereof.

14. The compound of claim 1 that is:

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-methoxy-1*H*-1,2,4-triazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-7-((1,3-dimethyl-5-oxo-1,5-dihydro-4*H*-1,2,4-triazol-4-yl)methyl)-6-fluoro-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((3-amino-1*H*-pyrazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-7-((3-(methoxymethyl)-1*H*-pyrazol-1-yl)methyl)-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((5-amino-1*H*-1,2,4-triazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-7-((3-amino-1*H*-1,2,4-triazol-1-yl)methyl)-4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-3,4-dihydroquinazolin-2(1*H*)-one;

(*S*)-1-((4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-2-oxo-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1*H*-1,2,4-triazole-3-carboxamide;

(*S*)-1-((4-(cyclopropylethynyl)-4-(1,1-difluoroethyl)-6-fluoro-2-oxo-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1*H*-1,2,4-triazole-5-carboxamide;

(*S*)-1-((4-(cyclopropylethynyl)-6-fluoro-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1*H*-1,2,4-triazole-5-carboxamide; or

(*S*)-1-((4-(cyclopropylethynyl)-6-fluoro-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-7-yl)methyl)-1*H*-1,2,4-triazole-3-carboxamide;

or a pharmaceutically acceptable salt thereof.

15. A pharmaceutical composition comprising an effective amount of the compound according to any one of claims 1 to 14, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

16. The pharmaceutical composition of claim 15 further comprising an effective amount of one or more additional nucleoside or nucleotide HIV reverse transcriptase inhibitors, nucleoside or nucleotide reverse transcriptase translocation inhibitors, non-nucleoside HIV reverse transcriptase inhibitors, HIV integrase inhibitors, HIV fusion inhibitors, HIV entry inhibitors, HIV maturation inhibitors, post-attachment inhibitors and latency reversing agents.

17. Use of the compound according to claim 1, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of infection by HIV, or for the treatment, prophylaxis or delay in the onset or progression of AIDS or ARC.

18. A compound according to claim 1, or a pharmaceutically acceptable salt thereof, for use in eliciting GAG-POL dimerization in HIV-infected cells in a human subject in need thereof.

19. A compound according to claim 1, or a pharmaceutically acceptable salt thereof, for use in selectively killing HIV infected GAG-POL expressing cells in a human subject.

20. A compound according to claim 1, or a pharmaceutically acceptable salt thereof, for use in selectively killing HIV infected GAG-POL expressing cells without concomitant cytotoxicity to HIV naïve cells in a human subject.

21. A compound according to claim 1, or a pharmaceutically acceptable salt thereof, for use in augmenting the suppression of HIV viremia in a human subject whose viremia is being suppressed by administration of one or more compatible HIV antiviral agents.

22. The use of claim 17 or the compound for use of of any one of claims 18 to 21 further comprising one or more additional compatible HIV antiviral agents selected from nucleoside or nucleotide HIV reverse transcriptase inhibitors, nucleoside reverse transcriptase translocation inhibitors, non-nucleoside HIV reverse transcriptase inhibitors, HIV integrase inhibitors, HIV fusion inhibitors, HIV entry inhibitors, HIV maturation inhibitors, post-attachment inhibitors and latency reversing agents.

23. The compound according to any one of claims 1 to 14 for use in therapy.