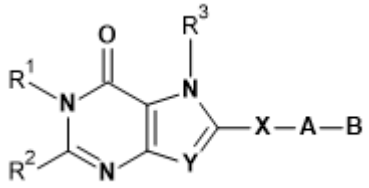
n is 0, 1, 2, 3 or 4, and p is 0, 1 or 2, in the manufacture of a medicament for the treatment of a condition or disorder ameliorated by inhibition of the A_{2A}/A_{2B} receptor; and the condition or disorder is selected from prostate cancer, rectal cancer, renal cancer, ovarian cancer, endometrial cancer, thyroid cancer, pancreatic cancer, breast cancer, colon cancer, bladder cancer, brain cancer, glial cancer, melanoma cancer, pineal gland cancer, or lung cancer.

[0019a] In another aspect, the present disclosure refers to use of the pharmaceutical composition as disclosed herein, in the manufacture of a medicament for the treatment of a disease or condition in a mammal that is amenable to treatment with an A_{2A}/A_{2B} receptor antagonist, and wherein the medicament is to be used in combination with at least one PD-L1 antibody for the treatment of a condition or disorder selected from prostate cancer, rectal cancer, renal cancer, ovarian cancer, endometrial cancer, thyroid cancer, pancreatic cancer, breast cancer, colon cancer, bladder cancer, brain cancer, glial cancer, melanoma cancer, pineal gland cancer, or lung cancer.

[0020] In yet another example, there is disclosed the use of a pharmaceutical composition comprising compound of Formula II and its pharmaceutically acceptable salts, analogs, and tautomeric forms thereof



Formula II

wherein,

Y is selected from N or CR; R is selected from H, hydroxy, alkoxy, alkyl, or aryl; R^1 is selected from a group consisting of alkyl, alkenyl and alkynyl, wherein one or more methylene groups are optionally replaced by hetero atoms or groupselected from –O-,-S(O)p-, -N(R^a)-, or -C(O) provided that the heteroatom is not adjacent to N in the ring; p is selected from 0, 1 or 2; wherein alkyl, alkenyl and alkynyl are unsubstituted or substituted independently with alkoxy, acyl, acylamino, acyloxy, amino, monoalkylamino, dialkylamino, aminocarbonyl, alkoxycarbonylamino, azido, cyano, halogen, haloalkyl, hydroxy, hydroxyalkyl, keto, thiocarbonyl, carboxy, alkylcarboxy, carboxyalkyl, -SO_3H, aminocarbonylamino, hydroxyamino, alkoxyamino, nitro, -$S(O)_2NR^aR^a$, -$NR^aS(O)_2R^a$, or -$S(O)_pR^a$; R^2 is selected from a group consisting of hydrogen, halogen, cyano, nitro, carboxy, acyl, aminocarbonyl, alkyl, alkenyl, alkynyl, hydroxyalkyl, carboxyalkyl, haloalkyl, haloalkyloxy, alkoxy, -NR^bR^b, -$S(O)_pR^b$, cycloalkyl, cycloalkylalkyl,

Example 3

Synthesis of the compound of Formula III and Formula IV

[00132] The compounds of Formula III or IV were synthesized as per the procedures mentioned in WO2012035548 which is incorporated herein by reference. Pharmaceutically acceptable salts of the compounds may be obtained as per procedures reported in literature.

[00133] The compounds of the disclosure may be prepared by a variety of methods, including standard synthetic chemistry. Any previously defined variable will continue to have the previously defined meaning unless otherwise indicated. Illustrative general synthetic methods are set out in the schemes and can be readily adapted to prepare other compounds of the disclosure.

Example 4

Biological Assay

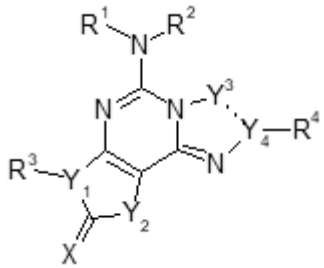
Tumor suppression activity of Adenosine A_{2A} (Compound 32) and A_{2B} (Compound 335) Antagonists in xenograft models of cancer

[00134] General Protocol: 6-8 weeks old BALB/c mice were acclimated and on Day 1 of the study, the mice were injected with 50 µL of medium containing 5 $X10^4$ 4T1 cells (breast cancer) or 5 X 10^5 CT26 cells (colon cancer). On day 8 or 9, the mice were segregated into different groups and treated orally with either vehicle (1% Tween-80+ 0.5% Carboxymethylcellulose in water) or test compound [(Compound 32 5-Amino-3-[2-[4-[2-fluoro-4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(32) &** Phosphoric acid mono-{2-cyano-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl} ester **(335)]** in vehicle. The treatment was BID for 22 days (colon cancer) or 28 days (breast cancer). At the end of the study, the tumor volume was measured as (length X breadth)/2. Data were presented as % reduction compared to the tumor volume in vehicle treated animals.

4T1 Breast Cancer Model	
Treatment Groups (n=12)	% decrease in Tumor growth *vs*. vehicle

I/We Claim:

1. Use of a pharmaceutical composition comprising compound of Formula I and its pharmaceutically acceptable salt, analog, and tautomeric form, thereof



Formula I

wherein

--- represents a single bond or a double bond;

X is selected from O, S or NR^a; Y_1 is selected from N or CH; Y_2 is selected from NR^5, O or CR^5R^6;

Y_3 is selected from N, CH, CH_2, C(=O), or C(=S); Y_4 is selected from N, C, or CH; R^1 and R^2 are independently selected from hydrogen or alkyl; R^3 is –A-Z-B-Q;

wherein, A is absent or is a group selected from alkylene, alkenylene, or alkynylene; wherein one or more methylene group is optionally replaced by hetero atoms or groups such as –O-, -S(O)p-, -N(R^a)-, or -C(O); alkylene, alkenylene and alkynylene is optionally substituted with -$(CR^dR^e)_nOR^7$, $(CR^dR^e)_nCOOR^7$, -$(CR^dR^e)_nNR^8R^9$, cyano, halogen, haloalkyl, perhaloalkyl, alkoxyalkoxy, alkyl, or cycloalkyl;

Z is absent or is selected from a cycloalkyl or a heterocyclyl; wherein cycloalkyl and heterocyclyl are unsubstituted or substituted independently with 1, 2, or 3 substituents independently selected from alkyl, alkenyl, alkynyl, acyl, -$(CR^dR^e)_nOR^7$, $(CR^dR^e)_nCOOR^7$, -$(CR^dR^e)_nNR^8R^9$, aminocarbonyl, alkoxycarbonylamino, halogen, haloalkyl, perhaloalkyl, azido, cyano, keto, thiocarbonyl, -SO_3H, aminocarbonylamino, nitro, -$S(O)_2NR^aR^a$, -$NR^bS(O)_2R^b$ or -$S(O)_pR^c$;

B is absent or is a group selected from alkylene, alkenylene or alkynylene; wherein one or more methylene groups is optionally replaced by hetero atoms or groups such as –O-, -S(O)p-, -N(R^a)-, or -C(O); alkylene, alkenylene and alkynylene is optionally substituted with hydroxy, amino, aminoalkyl, cyano, halogen, haloalkyl, perhaloalkyl, carboxy, carboxyalkyl, alkoxy, hydroxyalkyl, alkoxyalkyl, alkoxyalkoxy or alkyl;

Q is selected from hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl; wherein alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl are unsubstituted or substituted independently with 1, 2, or 3 substituents independently selected from alkyl, alkenyl, alkynyl, halogen, haloalkyl, perhaloalkyl, azido, cyano, nitro, keto, thiocarbonyl, cyanoalkyl, cyanoalkylcarbonyl, -$(CR^dR^e)_nOR^7$, -$(CR^dR^e)_nC(O)R^7$, -$(CR^dR^e)_nSR^7$, -$(CR^dR^e)_nCOOR^7$, -$(CR^dR^e)_nNR^8R^9$, -$(CR^dR^e)_nC(O)NR^8R^9$, -$(CR^dR^e)_nNR^8C(O)OR^7$, -$(CR^dR^e)_nNR^8C(O)NR^8R^9$, -$NR^bS(O)_2R^b$, -$S(O)_pR^c$, -$SO_3H$, -$S(O)_2NR^aR^a$, cycloalkyl, cycloalkenyl, cycloalkylalkyl aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl; wherein each substituent is unsubstituted or substituted with 1, 2, or 3 substituents independently selected from alkyl, carboxy, carboxyalkyl, aminocarbonyl, hydroxy, alkoxy, halogen, haloalkyl, perhaloalkyl, haloalkoxy, perhaloalkoxy, amino, substituted amino, cyano or -$S(O)_pR^c$;

R^4 is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, hydroxyalkyl, carboxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl; wherein alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, arylalkyl, aryl, heteroaryl, heteroarylalkyl, heterocyclyl, and heterocyclylalkyl are unsubstituted or substituted independently with up to four substituents independently selected from alkyl, alkenyl, alkynyl, acyl, -$(CR^dR^e)_nOR^7$, $(CR^dR^e)_nCOOR^7$, -$(CR^dR^e)_nNR^8R^9$, aminocarbonyl, alkoxycarbonylamino, aminocarbonylamino, azido, cyano, halogen,

haloalkyl, perhaloalkyl, keto, nitro, $-S(O)_2NR^bR^b$, $-NR^bS(O)_2R^b$ or $-S(O)_pR^c$, thiocarbonyl, $-SO_3H$, cycloalkyl, cycloalkenyl, aryl, heteroaryl or heterocyclyl;

R^5 and R^6 are independently selected from the group consisting of hydrogen, hydroxy, $-(CR^dR^e)_nOR^7$, $(CR^dR^e)_nCOOR^7$, $-(CR^dR^e)_nNR^8R^9$, cyanoalkyl, haloalkyl, alkoxyalkoxyalkyl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl;

R^7 is selected from hydrogen, alkyl, halogen, haloalkyl, $-(CR^dR^e)_nOR^7$, $-(CR^dR^e)_nCOOR^7$, $-(CR^eR^e)_nC(O)R^7$, carbonylamino, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, heterocyclyl or heterocyclylalkyl;

R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl, haloalkyl, $-(CR^dR^e)_nOR^7$, $-(CR^dR^e)_nC(O)R^7$, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl and heterocyclylalkyl, or

R^8 and R^9 taken together form a monocyclic or a bicyclic ring system which is saturated or partially unsaturated and optionally have additional heteroatoms selected from O, N or S, said ring system is further optionally substituted with 1 to 4 substituents independently selected from halo, alkyl, alkenyl, alkynyl, nitro, cyano, $-(CR^dR^e)_nOR^7$, $-(CR^dR^e)_nSR^7$, $-(CR^dR^e)_nNR^8R^9$, oxo, alkylsulfonyl, $-(CR^dR^e)_nCOOR^7$, $-(CR^dR^e)_nC(O)NR^8R^9$, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

R^a is selected from hydrogen or alkyl; R^b each is independently selected from the group consisting of hydrogen, alkyl, acyl, carboxyalkyl, carbonylamino, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, heterocyclyl and heterocyclylalkyl; R^c is selected from alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl; R^d and R^e are independently selected from the group consisting of hydrogen, $-OR^7$, halogen, haloalkyl, perhaloalkyl and alkyl;

n is 0, 1, 2, 3 or 4, and

p is 0, 1 or 2,

in the manufacture of a medicament for the treatment of a condition or disorder ameliorated by inhibition of the A_{2A}/A_{2B} receptor; and the condition or disorder is selected from prostate cancer, rectal cancer, renal cancer, ovarian cancer, endometrial cancer, thyroid cancer, pancreatic cancer, breast cancer, colon cancer, bladder cancer, brain cancer, glial cancer, melanoma cancer, pineal gland cancer, or lung cancer.

2. Use of the pharmaceutical composition as claimed in claim 1, in the manufacture of a medicament for the treatment of a disease or condition in a mammal that is amenable to treatment with an A_{2A}/A_{2B} receptor antagonist; and wherein the medicament is to be used in combination with at least one PD-L1 antibody for the treatment of a condition or disorder selected from prostate cancer, rectal cancer, renal cancer, ovarian cancer, endometrial cancer, thyroid cancer, pancreatic cancer, breast cancer, colon cancer, bladder cancer, brain cancer, glial cancer, melanoma cancer, pineal gland cancer, or lung cancer.
3. The use as claimed in claim 1, wherein the compound of Formula I is selected from the group consisting of:

5-Amino-8-(2-furyl)-3-[2-[4-[4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(1)**,

5-Amino-8-(2-furyl)-3-(2-hydroxyethyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(2)**,

5-Amino-3-[2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(3)**,

5-Amino-8-(2-furyl)-3-[2-[4-(4-methoxyphenyl)piperazin-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(4)**,

5-Amino-8-(2-furyl)-1-methyl-3-(2-morpholinoethyl)-[1,2,4]triazolo[5,1-f]purin-2-one **(5)**,

5-Amino-3-[2-[4-(2,4-difluorophenyl)-1-piperidyl]ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(6)**,

5-Amino-8-(2-furyl)-1-methyl-3-[2-[4-(5-methyl-2-pyridyl)piperazin-1-yl]ethyl]-[1,2,4]triazolo[5,1-f]purin-2-one **(7)**,
5-Amino-8-(2-furyl)-1-methyl-3-[2-[4-(p-tolyl)piperazin-1-yl]ethyl]-[1,2,4]triazolo[5,1-f]purin-2-one **(8)**,
5-Amino-8-(2-furyl)-1-methyl-3-[2-[4-(3-methyl-2-oxo-butyl)piperazin-1-yl]ethyl]-[1,2,4]triazolo[5,1-f]purin-2-one **(9)**,
5-Amino-3-[2-[4-(2-fluoro-4-methoxy-phenyl)piperazin-1-yl]ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(10)**,
5-Amino-8-(2-furyl)-3-[2-[4-[4-(2-methoxy-1,1-dimethyl-ethoxy)phenyl]piperazin-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(11)**,
5-Amino-8-(2-furyl)-3-[2-[4-(6-methoxy-3-pyridyl)piperazin-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(12)**,
5-Amino-3-[2-[4-[3-fluoro-4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(13)**,
5-Amino-8-(2-furyl)-3-[2-[4-[4-(1-hydroxy-1-methyl-ethyl)phenyl]piperazin-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(14)**,
5-Amino-3-[2-[4-(4-fluorophenyl)-4-hydroxy-1-piperidyl]ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(15)**,
5-Amino-8-(2-furyl)-3-[2-[4-[4-(2-methoxy-2-methyl-propoxy)phenyl]piperazin-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(16)**,
5-Amino-3-[2-[4-[4-(cyclopropoxy)phenyl]piperazin-1-yl]ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(17)**,
5-Amino-3-[2-[4-(4-fluorophenyl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(18)**,
5-Amino-8-(2-furyl)-3-[2-[4-hydroxy-4-(4-methoxyphenyl)-1-piperidyl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(19)**,
5-Amino-3-[2-[4-[3,5-difluoro-4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(20)**,

5-Amino-3-[2-[4-[2,5-difluoro-4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(21)**,
5-Amino-3-[2-[4-(2,2-difluoro-1,3-benzodioxol-5-yl)piperazin-1-yl]ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(22)**,
5-Amino-8-(2-furyl)-3-[2-[4-[4-(2-methoxyethoxy)phenyl]-3,3-dimethyl-piperazin-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(23)**,
5-Amino-3-[2-(4-butylpiperazin-1-yl)ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(24)**,
5-Amino-8-(2-furyl)-3-[2-(4-hydroxy-4-methyl-1-piperidyl)ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(25)**,
5-Amino-3-[2-[4-[4-[2-(cyclopropoxy)ethoxy]phenyl]piperazin-1-yl]ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(26)**,
5-Amino-8-(2-furyl)-3-[2-[4-[(4-methoxyphenyl)methyl]piperazin-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(27)**,
5-Amino-8-(2-furyl)-3-[2-[4-[[4-(2-methoxyethoxy)phenyl]methyl]piperazin-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(28)**,
5-Amino-8-(2-furyl)-3-[(4-methoxyphenyl)methyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(29)**,
5-Amino-8-(2-furyl)-3-[2-[4-(4-methoxyphenyl)piperazin-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(30)**,
5-Amino-8-(2-furyl)-3-[2-[4-[3-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(31)**,
5-Amino-3-[2-[4-[2-fluoro-4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(32)**,
4-[4-[2-[5-Amino-8-(2-furyl)-1-methyl-2-oxo-[1,2,4]triazolo[5,1-f]purin-3yl]ethyl]piperazin-1-yl]benzonitrile **(33)**,
4-[4-[2-[5-Amino-8-(2-furyl)-1-methyl-2-oxo-[1,2,4]triazolo[5,1-f]purin-3-yl]ethyl]piperazin-1-yl]-2-fluoro-benzonitrile **(34)**,
5-Amino-8-(2-furyl)-1-methyl-3-[2-[4-[4-(trifluoromethyl)phenyl]piperazin-1-yl]ethyl]-[1,2,4]triazolo[5,1-f]purin-2-one **(35)**,

5-Amino-8-(2-furyl)-1-methyl-3-[2-[4-[4-(trifluoromethyl)thiazol-2-yl]piperazin-1-yl]ethyl]-[1,2,4]triazolo[5,1-f]purin-2-one **(36)**,

5-Amino-3-[2-[4-(cyclopropylmethyl)piperazin-1-yl]ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(37)**,

5-Amino-3-[2-(4-ethylpiperazin-1-yl)ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(38)**,

4-[2-[5-Amino-8-(2-furyl)-1-methyl-2-oxo-[1,2,4]triazolo[5,1-f]purin-3-yl]ethyl]-N,N-dimethyl-piperazine-1-sulfonamide **(39)**,

5-Amino-8-(2-furyl)-1-methyl-3-[2-[4-(4-tetrahydrofuran-3-yloxyphenyl)piperazin-1-yl]ethyl]-[1,2,4]triazolo[5,1-f]purin-2-one **(40)**,

5-Amino-8-(2-furyl)-1-methyl-3-[2-[4-(4-tetrahydropyran-4-yloxyphenyl)piperazin-1-yl]ethyl]-[1,2,4]triazolo[5,1-f]purin-2-one **(41)**,

5-Amino-8-(2-furyl)-1-methyl-3-[2-[4-[4-(tetrahydrofuran-2-ylmethoxy)phenyl]piperazin-1-yl]ethyl]-[1,2,4]triazolo[5,1-f]purin-2-one **(42)**,

5-Amino-8-(2-furyl)-1-methyl-3-[2-(3-methyl-7,8-dihydro-5H-1,6-naphthyridin-6-yl)ethyl]-[1,2,4]triazolo[5,1-f]purin-2-one **(43)**,

5-Amino-3-[2-(6,7-dihydro-4H-thieno[3,2-c]pyridin-5-yl)ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(44)**,

5-Amino-8-(2-furyl)-3-[2-[4-[4-(2-methoxyethoxy)phenyl]piperazin-1-yl]propyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(45)**,

5-Amino-3-[2-[3-(4-fluorophenyl)-2,5-dihydropyrrol-1-yl]ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(46)**,

5-Amino-3-[2-[4-[4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-1-methyl-8-(5-methyl-2-furyl)-[1,2,4]triazolo[5,1-f]purin-2-one **(47)**,

5-Amino-8-(5-cyclopropyl-2-furyl)-3-[2-[4-[4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(48)**,

5-Amino-3-[2-(2,4-difluoroanilino)ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(49)**,

5-Amino-3-[3-[4-(4-fluorophenyl)piperazin-1-yl]propyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(50)**,

5-Amino-8-(2-furyl)-3-[3-[4-[4-(2-methoxyethoxy)phenyl]piperazin-1-yl]propyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(51)**,
5-Amino-8-(2-furyl)-3-[2-[4-(4-methoxyphenyl)-3,6-dihydro-2H-pyridin-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(52)**,
5-Amino-8-(2-furyl)-3-[2-[4-[4-(2-methoxy-1,1-dimethyl-ethyl)phenyl]piperazin-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(53)**,
5-Amino-8-(2-furyl)-1-methyl-3-(2-piperazin-1-ylethyl)-[1,2,4]triazolo[5,1-f]purin-2-one **(54)**,
5-Amino-8-(2-furyl)-3-[2-[4-(1H-indole-2-carbonyl)piperazin-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(55)**,
5-Amino-8-(2-furyl)-3-[2-(4-isopropoxyphenyl)ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(56)**,
5-Amino-8-(2-furyl)-1-methyl-3-[2-[4-[(2S)-pyrrolidine-2-carbonyl]piperazin-1-yl]ethyl]-[1,2,4]triazolo[5,1-f]purin-2-one **(57)**,
5-Amino-8-(2-furyl)-3-[2-(4-methoxyphenyl)ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(58)**,
5-amino-3-[2-[4-[4-(difluoromethoxy)phenyl]piperazin-1-yl]ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(59)**,
5-Amino-8-(2-furyl)-1-methyl-3-[2-[4-[3-(5-methyl-1,3,4-oxadiazol-2-yl)phenyl]piperazin-1-yl]ethyl]-[1,2,4]triazolo[5,1-f]purin-2-one **(60)**,
5-Amino-3-[2-[4-[2-fluoro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]piperazin-1-yl]ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(61)**,
5-Amino-3-[2-[4-(6-fluoro-2-methyl-1,3-benzoxazol-5-yl)piperazin-1-yl]ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(62)**,
5-Amino-3-[2-[4-(cyclopropanecarbonyl)piperazin-1-yl]ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(63)**,
5-Amino-3-[2-[4-(2-cyclopropylacetyl)piperazin-1-yl]ethyl]-8-(2-furyl)-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(64)**,

5-Amino-8-(2-furyl)-3-[2-[4-[4-(2-hydroxyethoxy)phenyl]piperazin-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(65)**,
5-Amino-8-(2-furyl)-3-[2-[4-(4-hydroxyphenyl)piperazin-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(66)**,
5-Amino-1-(cyclopropylmethyl)-3-[2-[4-(4-ethoxyphenyl)piperazin-1-yl]ethyl]-8-(2-furyl)-[1,2,4]triazolo[5,1-f]purin-2-one **(67)**,
5-Amino-1-(cyclopropylmethyl)-3-[2-[4-(4-fluorophenyl)piperazin-1-yl]ethyl]-8-(2-furyl)-[1,2,4]triazolo[5,1-f]purin-2-one **(68)**,
5-Amino-1-(cyclopropylmethyl)-3-[2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl]-8-(2-furyl)-[1,2,4]triazolo[5,1-f]purin-2-one **(69)**,
5-Amino-1-(cyclopropylmethyl)-8-(2-furyl)-3-[2-[4-[4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-[1,2,4]triazolo[5,1-f]purin-2-one **(70)**,
5-Amino-1-(cyclopropylmethyl)-3-[2-(4-fluorophenoxy)ethyl]-8-(2-furyl)-[1,2,4]triazolo[5,1-f]purin-2-one **(71)**,
5-Amino-8-(2-furyl)-1-methyl-3-[2-[2-oxo-5-(trifluoromethyl)-1-pyridyl]ethyl]-[1,2,4]triazolo[5,1-f]purin-2-one **(72)**,
5-Amino-3-[2-[4-(2,4-difluorophenyl)pyrazol-1-yl]ethyl]-1-ethyl-8-(2-furyl)-[1,2,4]triazolo[5,1-f]purin-2-one **(73)**,
1-[2-[5-Amino-1-(cyclopropylmethyl)-8-(2-furyl)-2-oxo-[1,2,4]triazolo[5,1-f]purin-3-yl]ethyl]pyrazole-4-carboxylic acid **(74)**,
1-[2-[5-Amino-8-(2-furyl)-1-methyl-2-oxo-[1,2,4]triazolo[5,1-f]purin-3-yl]ethyl]pyrazole-4-carboxylic acid **(75)**,
1-[2-[5-amino-1-(cyclopropylmethyl)-8-(2-furyl)-2-oxo-[1,2,4]triazolo[5,1-f]purin-3-yl]ethyl]-N-cyclopropyl-pyrazole-4-carboxamide **(76)**,
1-[2-[5-amino-1-(cyclopropylmethyl)-8-(2-furyl)-2-oxo-[1,2,4]triazolo[5,1-f]purin-3-yl]ethyl]-N,N-diethyl-pyrazole-4-carboxamide **(77)**,
1-[2-[5-Amino-1-(cyclopropylmethyl)-8-(2-furyl)-2-oxo-[1,2,4]triazolo[5,1-f]purin-3-yl]ethyl]-N-cyclopropyl-5-methyl-pyrazole-3-carboxamide **(78)**,
2-[2-[5-Amino-1-(cyclopropylmethyl)-8-(2-furyl)-2-oxo-[1,2,4]triazolo[5,1-f]purin-3-yl]ethyl]-N-cyclopropyl-5-methyl-pyrazole-3-carboxamide **(79)**,

1-[2-[5-Amino-8-(2-furyl)-1-methyl-2-oxo-[1,2,4]triazolo[5,1-f]purin-3-yl]ethyl]-N-methyl-pyrazole-3-carboxamide **(80)**,
1-[2-[5-Amino-8-(2-furyl)-1-methyl-2-oxo-[1,2,4]triazolo[5,1-f]purin-3-yl]ethyl]-N,N-diethyl-pyrazole-4-carboxamide **(81)**,
1-[2-[5-amino-8-(2-furyl)-1-methyl-2-oxo-[1,2,4]triazolo[5,1-f]purin-3-yl]ethyl]pyrazole-4-carboxamide **(82)**,
5-Amino-8-(2-furyl)-3-[2-[4-[(3R)-3-hydroxypyrrolidine-1-carbonyl]pyrazol-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(83)**,
1-[2-[5-Amino-8-(2-furyl)-1-methyl-2-oxo-[1,2,4]triazolo[5,1-f]purin-3-yl]ethyl]-N-methyl-pyrazole-4-carboxamide **(84)**,
1-[2-[5-Amino-8-(2-furyl)-1-methyl-2-oxo-[1,2,4]triazolo[5,1-f]purin-3-yl]ethyl]-N-cyclopropyl-pyrazole-3-carboxamide **(85)**,
1-[2-[5-Amino-8-(2-furyl)-1-methyl-2-oxo-[1,2,4]triazolo[5,1-f]purin-3-yl]ethyl]-N-cyclopropyl-pyrazole-4-carboxamide **(86)**,
5-Amino-8-(2-furyl)-3-[2-[4-(3-hydroxyazetidine-1-carbonyl)pyrazol-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(87)**,
5-Amino-1-ethyl-8-(2-furyl)-3-[2-[4-[4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-[1,2,4]triazolo[5,1-f]purin-2-one **(88)**,
5-Amino-3-[2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl]-1-ethyl-8-(2-furyl)-[1,2,4]triazolo[5,1-f]purin-2-one **(89)**,
5-Amino-1-ethyl-3-{2-[4-(4-fluoro-phenyl)-piperidin-1-yl]-ethyl}-8-furan-2-yl-1,3-dihydro-[1,2,4]triazolo[5,1-f]purin-2-one **(90)**,
5-Amino-1-ethyl-8-(2-furyl)-3-[2-(3-methyl-7,8-dihydro-5H-1,6-naphthyridin-6-yl)ethyl]-[1,2,4]triazolo[5,1-f]purin-2-one **(91)**,
5-Amino-8-(2-furyl)-3-[2-[4-[4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-1-(2,2,2-trifluoroethyl)-[1,2,4]triazolo[5,1-f]purin-2-one **(92)**,
5-Amino-3-{2-[4-(2,4-difluoro-phenyl)-piperazin-1-yl]-ethyl}-8-furan-2-yl-1-(2,2,2-trifluoro-ethyl)-1,3-dihydro-[1,2,4]triazolo[5,1-f]purin-2-one **(93)**,
5-Amino-8-(2-furyl)-3-[2-[4-[4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-1-(2-methoxyethyl)-[1,2,4]triazolo[5,1-f]purin-2-one **(94)**,

5-amino-3-[2-[4-(4-fluorophenyl)piperazin-1-yl]ethyl]-8-(2-furyl)-1-(2-methoxyethyl)-[1,2,4]triazolo[5,1-f]purin-2-one **(95)**,
5-Amino-3-[2-[4-(4-fluorophenyl)piperazin-1-yl]ethyl]-8-(2-furyl)-1-(2-hydroxyethyl)-[1,2,4]triazolo[5,1-f]purin-2-one one **(96)**,
5-Amino-1-cyclopropyl-8-(2-furyl)-3-[2-[4-[4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-[1,2,4]triazolo[5,1-f]purin-2-one **(97)**,
5-Amino-8-(2-furyl)-3-[2-[4-[4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-1-(2,2,2-trifluoroethyl)-[1,2,4]triazolo[5,1-f]purin-2-one **(98)**,
5-Amino-3-[2-[4-[4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-1-methyl-8-thiazol-2-yl-[1,2,4]triazolo[5,1-f]purin-2-one **(99)**,
5-Amino-3-[2-[4-[3-fluoro-4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-1-methyl-8-thiazol-2-yl-[1,2,4]triazolo[5,1-f]purin-2-one **(100)**,
5-Amino-3-[2-[4-(2-cyclopropylacetyl)piperazin-1-yl]ethyl]-1-methyl-8-thiazol-2-yl-[1,2,4]triazolo[5,1-f]purin-2-one **(101)**,
5-Amino-3-[2-[4-(4-methoxyphenyl)piperazin-1-yl]ethyl]-1-methyl-8-thiazol-2-yl-[1,2,4]triazolo[5,1-f]purin-2-one **(102)**,
5-Amino-1-methyl-3-[2-[4-(p-tolyl)piperazin-1-yl]ethyl]-8-thiazol-2-yl-[1,2,4]triazolo[5,1-f]purin-2-one **(103)**,
5-Amino-1-methyl-3-[2-(3-methyl-7,8-dihydro-5H-1,6-naphthyridin-6-yl)ethyl]-8-thiazol-2-yl-[1,2,4]triazolo[5,1-f]purin-2-one **(104)**,
4-[4-[2-(5-Amino-1-methyl-2-oxo-8-thiazol-2-yl-[1,2,4]triazolo[5,1-f]purin-3-yl)ethyl]piperazin-1-yl]benzonitrile **(105)**,
5-Amino-1-methyl-3-[2-[4-[3-(5-methyl-1,3,4-oxadiazol-2-yl)phenyl]piperazin-1-yl]ethyl]-8-thiazol-2-yl-[1,2,4]triazolo[5,1-f]purin-2-one **(106)**,
5-amino-3-[2-[4-[4-(1-hydroxy-1-methyl-ethyl)phenyl]piperazin-1-yl]ethyl]-1-methyl-8-thiazol-2-yl-[1,2,4]triazolo[5,1-f]purin-2-one **(107)**,
5-Amino-3-[2-[4-[4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-1-methyl-8-(2-pyridyl)-[1,2,4]triazolo[5,1-f]purin-2-one **(108)**,

5-Amino-3-[2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl]-1-methyl-8-(2-pyridyl)-[1,2,4]triazolo[5,1-f]purin-2-one **(109)**,
4-[4-[2-[5-Amino-1-methyl-2-oxo-8-(2-pyridyl)-[1,2,4]triazolo[5,1-f]purin-3-yl]ethyl]piperazin-1-yl]benzonitrile **(110)**,
5-Amino-3-[2-[4-[4-(1-hydroxy-1-methyl-ethyl)phenyl]piperazin-1-yl]ethyl]-1-methyl-8-(2-pyridyl)-[1,2,4]triazolo[5,1-f]purin-2-one **(111)**,
5-Amino-3-[2-[4-[4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-1-methyl-8-pyrazin-2-yl-[1,2,4]triazolo[5,1-f]purin-2-one **(112)**,
5-Amino-3-[2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl]-1-methyl-8-pyrazin-2-yl-[1,2,4]triazolo[5,1-f]purin-2-one **(113)**,
5-Amino-3-[2-[4-[2-fluoro-4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-1-methyl-8-pyrazin-2-yl-[1,2,4]triazolo[5,1-f]purin-2-one **(114)**,
5-Amino-8-(2-furyl)-3-[[1-(4-methoxyphenyl)pyrrolidin-3-yl]methyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(115)**,
5-Amino-8-(2-furyl)-3-[[1-[4-(2-methoxyethoxy)phenyl]pyrrolidin-3-yl]methyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-onehyl}-1-methyl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(116)**,
5-amino-8-(2-furyl)-3-[2-[4-[4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purine-2-thione **(117)**,
8-(2-furyl)-3-[2-[4-[4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-1-methyl-5-(methylamino)-[1,2,4]triazolo[5,1-f]purin-2-one **(118)**,
5-Amino-3-{2-[4-(4-fluoro-phenyl)-piperazin-1-yl]-ethyl}-8-isothiazol-5-yl-1-methyl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(119)**,
5-Amino-8-isothiazol-5-yl-3-(2-{4-[4-(2-methoxy-ethoxy)-phenyl]-piperazin-1-yl}-ethyl)-1-methyl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(120)**,
5-Amino-3-[2-[4-[2-fluoro-4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-8-isothiazol-5-yl-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(121)**,
5-Amino-8-isoxazol-5-yl-3-[2-[4-[4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-1-methyl-[1,2,4]triazolo[5,1-f]purin-2-one **(122)**,
5-Amino-3-[2-[4-[4-(2-methoxyethoxy)phenyl]piperazin-1-yl]ethyl]-1-methyl-8-oxazol-2-yl-[1,2,4]triazolo[5,1-f]purin-2-one **(123)**,

5-Amino-3-{2-[4-(4-methoxy-phenyl)-piperazin-1-yl]-ethyl}-1-methyl-8-prop-1-ynyl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(124)**,
5-Amino-3-(2-{4-[4-(2-methoxy-ethoxy)-phenyl]-piperazin-1-yl}-ethyl)-1-methyl-8-prop-1-ynyl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(125)**,
5-Amino-3-{2-[4-(4-fluoro-benzoyl)-piperazin-1-yl]-ethyl}-8-furan-2-yl-1-methyl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(126)**,
5-Amino-3-(2-dimethylamino-ethyl)-8-furan-2-yl-1-methyl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(127)**,
5-Amino-8-furan-2-yl-3-[3-(4-methoxy-phenyl)-propyl]-1-methyl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(128)**,
5-Amino-8-furan-2-yl-1-methyl-3-(2-pyrazol-1-yl-ethyl)-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(129)**,
5-Amino-8-furan-2-yl-3-(2-{4-[4-(2-methoxy-ethoxy)-phenyl]-pyrazol-1-yl}-ethyl)-1-methyl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(130)**,
5-Amino-8-furan-2-yl-3-{2-[3-(4-methoxy-phenyl)-pyrrol-1-yl]-ethyl}-1-methyl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(131)**,
5-Amino-8-furan-2-yl-3-{2-[4-(4-methoxy-phenyl)-imidazol-1-yl]-ethyl}-1-methyl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(132)**,
5-Amino-8-furan-2-yl-3-{2-[4-(4-methoxy-phenyl)-[1,2,3]triazol-1-yl]-ethyl}-1-methyl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(133)**,
5-Amino-3-[2-(1,3-dihydro-isoindol-2-yl)-ethyl]-8-furan-2-yl-1-methyl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(134)**,
5-Amino-8-furan-2-yl-1-methyl-3-(2-piperidin-1-yl-ethyl)-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(135)**,
5-Amino-8-furan-2-yl-1-methyl-3-(2-pyrrolidin-1-yl-ethyl)-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(136)**,
5-Amino-8-furan-2-yl-1-methyl-3-[2-(3-methyl-7,8-dihydro-5H-[1,6]naphthyridin-6-yl)-ethyl]-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(137)**,
5-Amino-8-furan-2-yl-3-{2-[4-(2-methoxy-ethoxy)-phenoxy]-ethyl}-1-methyl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(138)**,

5-Amino-8-furan-2-yl-3-{2-[4-(2-methoxy-ethoxy)-phenylamino]-ethyl}-1-methyl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(139)**,
5-Amino-8-furan-2-yl-1-methyl-3-[2-(pyridin-2-yloxy)-ethyl]-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(140)**,
5-Amino-1-ethyl-3-{2-[4-(4-fluoro-phenyl)-piperazin-1-yl]-ethyl}-8-isothiazol-5-yl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(141)**,
5-Amino-1-ethyl-8-isothiazol-5-yl-3-(2-{4-[4-(2-methoxy-ethoxy)-phenyl]-piperazin-1-yl}-ethyl)-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(142)**,
5-Amino-1-ethyl-8-furan-2-yl-3-(2-piperidin-1-yl-ethyl)-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(143)**,
5-Amino-1-ethyl-8-furan-2-yl-3-[2-(3-methyl-7,8-dihydro-5H-[1,6]naphthyridin-6-yl)-ethyl]-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(144)**,
5-Amino-3-[2-(2,4-difluoro-phenoxy)-ethyl]-1-ethyl-8-furan-2-yl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(145)**,
5-Amino-3-[2-(2,4-difluoro-phenylamino)-ethyl]-1-ethyl-8-furan-2-yl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(146)**,
5-Amino-1-cyclopropylmethyl-3-[2-(2,4-difluoro-phenylamino)-ethyl]-8-furan-2-yl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(147)**,
5-Amino-1-cyclopropylmethyl-3-[2-(2,4-difluoro-phenoxy)-ethyl]-8-furan-2-yl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(148)**,
5-Amino-1-cyclopropylmethyl-3-{2-[4-(4-fluoro-phenyl)-piperidin-1-yl]-ethyl}-8-furan-2-yl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(149)**,
5-Amino-3-{2-[4-(4-fluoro-phenyl)-piperidin-1-yl]-ethyl}-8-furan-2-yl-1-(2,2,2-trifluoro-ethyl)-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(150)**,
5-Amino-8-furan-2-yl-3-{2-[4-(4-methoxy-phenyl)-piperazin-1-yl]-ethyl}-1-(2,2,2-trifluoro-ethyl)-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(151)**,
5-Amino-3-[2-(4-cyclopropylmethyl-piperazin-1-yl)-ethyl]-8-isothiazol-5-yl-1-(2,2,2-trifluoro-ethyl)-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(152)**,

(5-Amino-8-isothiazol-5-yl-3-{2-[4-(4-methoxy-phenyl)-piperazin-1-yl]-ethyl}-2-oxo-2,3-dihydro-[1,2,4]triazolo[5,1-i]purin-1-yl)-acetonitrile **(153)**,

[5-Amino-3-{2-[4-(2,4-difluoro-phenyl)-piperazin-1-yl]-ethyl}-8-(3-fluoro-phenyl)-2-oxo-2,3-dihydro-[1,2,4]triazolo[5,1-i]purin-1-yl]-acetonitrile **(154)**,

[5-Amino-8-furan-2-yl-3-(2-{4-[4-(2-methoxy-ethoxy)-phenyl]-piperazin-1-yl}-ethyl)-2-oxo-2,3-dihydro-[1,2,4]triazolo[5,1-i]purin-1-yl]-acetonitrile **(155)**,

5-Amino-3-(2-{4-[4-(2-methoxy-ethoxy)-phenyl]-piperazin-1-yl}-ethyl)-1-methyl-8-phenyl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(156)**,

3-[5-Amino-3-(2-{4-[4-(2-methoxy-ethoxy)-phenyl]-piperazin-1-yl}-ethyl)-1-methyl-2-oxo-2,3-dihydro-1H-[1,2,4]triazolo[5,1-i]purin-8-yl]-benzonitrile **(157)**,

3-[5-Amino-3-(2-{4-[4-(2-methoxy-ethoxy)-phenyl]-piperazin-1-yl}-ethyl)-1-methyl-2-oxo-2,3-dihydro-1H-[1,2,4]triazolo[5,1-i]purin-8-yl]-benzonitrile **(158)**,

5-Amino-8-furan-2-yl-1-methyl-3-vinyl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(159)**

5-Amino-3-[3-(4-fluoro-phenyl)-prop-2-ynyl]-8-furan-2-yl-1-methyl-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(160)**,

5-Amino-8-furan-2-yl-1-methyl-3-[4-(4-methyl-piperazin-1-yl)-but-2-ynyl]-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(161)**,

5-Amino-8-furan-2-yl-1-isopropyl-3-(2-{4-[4-(2-methoxy-ethoxy)-phenyl]-piperazin-1-yl}-ethyl)-1,3-dihydro-[1,2,4]triazolo[5,1-i]purin-2-one **(162)**,

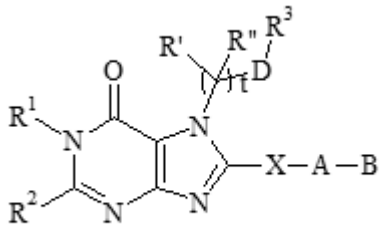
5-Amino-2-benzyl-7-(2-{4-[4-(2-methoxy-ethoxy)-phenyl]-piperazin-1-yl}-ethyl)-9-methyl-7,9-dihydro-2H-[1,2,4]triazolo[3,4-i]purine-3,8-dione **(163)**,

5-Amino-2-benzyl-9-methyl-7-(2-morpholin-4-yl-ethyl)-7,9-dihydro-2H-[1,2,4]triazolo[3,4-i]purine-3,8-dione **(164)**,

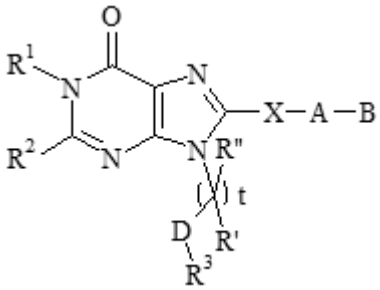
5-Amino-2-(3-chloro-benzyl)-7-[2-(4-isopropyl-piperazin-1-yl)-ethyl]-9-methyl-7,9-dihydro-2H-[1,2,4]triazolo[3,4-i]purine-3,8-dione **(165)**,

5-Amino-2-cyclopropylmethyl-9-methyl-7-(2-morpholin-4-yl-ethyl)-7,9-dihydro-2H-[1,2,4]triazolo[3,4-i]purine-3,8-dione **(166)**, 5-Amino-2-cyclopropylmethyl-7-(2,4-difluoro-benzyl)-9-methyl-7,9-dihydro-2H-[1,2,4]triazolo[3,4-i]purine-3,8-dione **(167)**, 4-Amino-2-furan-2-yl-6-(2-{4-[4-(2-methoxy-ethoxy)-phenyl]-piperazin-1-yl}-ethyl)-6H-8-oxa-1,3,3a,5,6-pentaaza-as-indacen-7-one **(168)**, and 4-Amino-2-furan-2-yl-6-(2-{4-[4-(2-methoxy-ethoxy)-phenyl]-piperazin-1-yl}-ethyl)-8,8-dimethyl-6,8-dihydro-1,3,3a,5,6-pentaaza-as-indacen-7-one **(169)**.

4. Use of a pharmaceutical composition comprising compound of Formula III or IV and its pharmaceutically acceptable salts, analogs, and tautomeric forms thereof



Formula III



Formula IV

wherein,

R^1 is an alkyl wherein one or more methylene groups are optionally replaced by hetero atoms or group selected from –O-, -S(O)p-, -N(R^a)-, or -C(O), provided that the heteroatom is not adjacent to N in the ring; p is selected from 0, 1 or 2;

wherein alkyl is unsubstituted or substituted with alkoxy, acyl, acylamino, acyloxy, amino, monoalkylamino, dialkylamino, aminocarbonyl, alkoxycarbonylamino, azido, cyano, halogen, haloalkyl, hydroxy, hydroxyalkyl, keto, thiocarbonyl, carboxy, alkylcarboxy, carboxyalkyl, -aminocarbonylamino, hydroxyamino, alkoxyamino;

R^2 is selected from the group consisting of hydrogen, halogen, cyano, nitro, carboxy, acyl, aminocarbonyl, alkyl, alkenyl, alkynyl, hydroxyalkyl, carboxyalkyl, haloalkyl, haloalkyloxy, alkoxy, $-NR^bR^b$, $-S(O)_pR^b$, cycloalkyl, cycloalkylalkyl, cycloalkyloxy, aryl, arylalkyl, aryloxy, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, heteroaryl, heteroarylalkyl and heteroaryloxy; wherein alkyl, alkenyl, alkynyl, alkoxy, carboxyalkyl, cycloalkyl, cycloalkylalkyl, cycloalkyloxy, aryl, arylalkyl, aryloxy, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, heteroaryl, heteroarylalkyl, heteroaryloxy and R^b are unsubstituted or substituted independently with alkyl, alkenyl, alkynyl, alkoxy, acyl, acylamino, acyloxy, nitro, amino, monoalkylamino, dialkylamino, hydroxyamino, alkoxyamino, aminocarbonylamino, azido, cyano, halogen, hydroxy, hydroxyalkyl, keto, thiocarbonyl, carboxy, alkylcarboxy, carboxyalkyl, $-SO_3H$, arylamino, cycloalkylamino, heteroarylamino, heterocyclylamino, aminocarbonyl, alkoxycarbonylamino, cycloalkyl, cycloalkyloxy, cycloalkenyl, aryl, aryloxy, heteroaryl, heteroaryloxy, heterocyclyl, heterocyclyloxy, $-S(O)_2NR^cR^c$, $-NR^cS(O)_2R^c$ or $-S(O)_pR^d$; wherein each substituent is unsubstituted or substituted with 1, 2, or 3 substituents independently selected from alkyl, carboxy, carboxyalkyl, aminocarbonyl, hydroxy, alkoxy, halogen, haloalkyl, haloalkoxy, amino, substituted amino, cyano or $-S(O)_pR^d$;

R' and R" are independently selected from hydrogen, or alkyl; or

R' and R" taken together may represent O, or a lower cycloalkyl ring system which is saturated or partially unsaturated;

R^3 is selected from the group consisting of alkyl, aryl, $-C(O)R^4$ and $-P(O)(OR^5)_2$;

R^4 is selected from alkyl, alkoxy, aryl, heteroaryl, heterocyclyl, or -NR^6R^7;

R^5 is selected from hydrogen, alkyl, aryl, arylalkyl, -$CH_2OC(O)$alkyl, or -$CH_2OC(O)O$alkyl; or two R^5 groups taken together form a five or six membered ring system which is saturated or partially unsaturated and is optionally substituted with 1 to 4 substituents independently selected from halo, alkyl, aryl or heteroaryl;

R^6 and R^7 are independently selected from the group consisting of hydrogen, alkyl, heterocyclyl and heterocyclylalkyl; or

R^6 and R^7 taken together form a monocyclic ring system which is saturated or partially unsaturated and optionally have additional heteroatoms selected from O, N or S, wherein the ring system is optionally substituted with 1 to 4 substituents independently selected from halo, alkyl, alkoxy, or -NR^8R^9;

R^4, R^5, R^6 and R^7 is optionally substituted with 1 to 4 substituents independently selected from hydroxyl, halogen, alkyl, alkoxy, haloalkyl, -NR^8R^9, -$C(O)OR^{10}$, -$OC(O)R^{10}$ or -$NC(O)R^{10}$;

R^8 and R^9 are independently selected from the group consisting of hydrogen and alkyl;

R^{10} is selected from hydrogen, hydroxy, halogen, amino, substituted amino, cyano, alkyl, alkoxy, haloalkyl, haloalkoxy, carboxy, carboxyalkyl, aminocarbonyl, aryl or arylalkyl;

X is an optionally substituted arylene or an optionally substituted heteroarylene;

A is selected from a bond, or (C_1-C_6)alkylene, wherein 1 to 4 methylene groups are optionally replaced by group independently selected from O, -$S(O)_p$-, -$N(R^b)$-, or -C(O)-; wherein alkylene is unsubstituted or substituted independently with alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, cycloalkenyl, acyl, acylamino, acyloxy, amino, monoalkylamino, dialkylamino, arylamino, cycloalkylamino, heteroarylamino, heterocyclylamino, aminocarbonyl, alkoxycarbonylamino, azido, cyano, halogen, hydroxy, hydroxyalkyl, keto, thiocarbonyl, carboxy, alkylcarboxy, carboxyalkyl, carboxyalkyloxy, alkylcarboxyalkyloxy -SO_3H, aryl, aryloxy,

cycloalkyloxy, heteroaryl, aminocarbonylamino, heteroaryloxy, heterocyclyl, heterocyclyloxy, hydroxyamino, alkoxyamino, nitro, $S(O)_2NR^cR^c$, $-NR^cS(O)_2R^c$ or $-S(O)_pR^d$;

wherein each substituent is unsubstituted or substituted with 1, 2, or 3 substituents independently selected from alkyl, carboxy, carboxyalkyl, aminocarbonyl, hydroxy, alkoxy, halogen, CF_3, amino, substituted amino, cyano or $-S(O)_pR^d$;

B is selected from hydrogen, heterocyclyl, cycloalkyl, aryl or heteroaryl; wherein heterocyclyl, cycloalkyl, aryl and heteroaryl are unsubstituted or substituted independently with alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, cycloalkylalkyl, cycloalkenyl, acyl, acylamino, acyloxy, amino, monoalkylamino, dialkylamino, arylamino, cycloalkylamino, heteroarylamino, heterocyclylamino, aminocarbonyl, alkoxycarbonylamino, azido, cyano, halogen, hydroxy, hydroxyalkyl, keto, thiocarbonyl, carboxy, alkylcarboxy, carboxyalkyl, carboxyalkyloxy, alkylcarboxyalkyloxy $-SO_3H$, aryl, arylalkyl, aryloxy, cycloalkyloxy, heteroaryl, heteroarylalkyl, aminocarbonylamino, heteroaryloxy, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, hydroxyamino, alkoxyamino, nitro, $-S(O)_2NR^bR^b$, $-NR^bS(O)_2R^b$ or $-S(O)_pR^d$; wherein each substituent is unsubstituted or substituted with 1, 2, or 3 substituents independently selected from alkyl, carboxy, carboxyalkyl, aminocarbonyl, hydroxy, alkoxy, alkoxyalkoxy, alkoxyalkyl, halogen, haloalkyl, haloalkoxy, amino, substituted amino, cyano or $-S(O)_pR^d$;

D is selected from –O-, -S(O)p-, or $-N(R^a)-$;

R^a is hydrogen or an alkyl;

R^b is selected from the group consisting of hydrogen, alkyl, acyl, carboxyalkyl, carbonylamino, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, heterocyclyl and heterocyclylalkyl;

R^c is selected from hydrogen, alkyl, aryl, heteroaryl or heterocyclyl;

R^d is selected from alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl;

p is 0, 1 or 2; and

t is 1 or 2, in the manufacture of a medicament for the treatment of a condition or disorder ameliorated by inhibition of the A_{2A}/A_{2B} receptor, wherein the condition or disorder is selected from prostate cancer, rectal cancer, renal cancer, ovarian cancer, endometrial cancer, thyroid cancer, pancreatic cancer, breast cancer, colon cancer, bladder cancer, brain cancer, glial cancer, melanoma cancer, pineal gland cancer, or lung cancer.

5. Use of the pharmaceutical composition as claimed in claim 4, in the manufacture of a medicament for the treatment of a disease or condition in a mammal that is amenable to treatment with an A_{2A}/A_{2B} receptor antagonist, wherein the medicament is to be used in combination with at least one PD-L1 antibody for the treatment of a condition or disorder selected from prostate cancer, rectal cancer, renal cancer, ovarian cancer, endometrial cancer, thyroid cancer, pancreatic cancer, breast cancer, colon cancer, bladder cancer, brain cancer, glial cancer, melanoma cancer, pineal gland cancer, or lung cancer.
6. The use as claimed in claim 4, wherein the compound of Formula III or Formula IV is selected from the group consisting of:
   Phosphoric acid mono-{2-cyano-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl} ester **(335)**,
   Phosphoric acid mono-{2-cyano-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-9-ylmethyl} ester di sodium salt **(336)**,
   Phosphoric acid mono-{2-chloro-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl} ester **(337)**,
   Phosphoric acid mono-{2-chloro-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-9-ylmethyl} ester **(338)**,
   2,2-Dimethyl-propionic acid 6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl ester **(339)**,
   2,2-Dimethyl-propionic acid 6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-9-ylmethyl ester **(340)**,

2,2-Dimethyl-propionic acid 2-chloro-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl ester **(341)**,

7-Methoxymethyl-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,7-dihydro-purin-6-one **(342)**,

9-Methoxymethyl-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,9-dihydro-purin-6-one **(343)**,

2-Chloro-7-methoxymethyl-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1, 7-dihydro-purin-6-one **(344)**,

Phosphoric acid mono-{6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl} ester **(345)**,

(2-Dimethylamino-ethyl)-methyl-carbamic acid 6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl ester **(346)**,

(1-Ethyl-pyrrolidin-2-ylmethyl)-carbamic acid 6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl ester **(347)**,

Nicotinic acid 6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl ester **(348)**,

Acetic acid 6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl ester **(349)**,

Butyric acid 6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl ester **(350)**,

Butyric acid 2-chloro-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl ester **(351)**,

Nicotinic acid 2-chloro-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl ester **(352)**,

(2-Dimethylamino-ethyl)-methyl-carbamic acid 2-chloro-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl ester **(353)**,

(2-Dimethylamino-ethyl)-methyl-carbamic acid 2-cyano-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl ester **(354)**,

Butyric acid 2-cyano-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl ester **(355)**,

2,2-Dimethyl-propionic acid 2-cyano-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl ester **(356)**,

Nicotinic acid 2-cyano-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl ester **(357)**,

4-Methyl-piperazine-1-carboxylic acid 2-cyano-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl ester **(358)**,

1-{6-Oxo-7-phosphonooxymethyl-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-6,7-dihydro-1H-purin-2-yl}-pyrrolidine-2-carboxylic acid **(359)**,

1-{7-(2,2-Dimethyl-propionyloxymethyl)-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-6,7-dihydro-1H-purin-2-yl}-pyrrolidine-2-carboxylic acid **(360)**,

2,2-Dimethyl-propionic acid 2-cyclopropyl-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl ester **(361)**,

Phosphoric acid mono-{2-cyclopropyl-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl} ester **(362)**,

Phosphoric acid mono-{2-chloro-6-oxo-1-propyl-8-[1-(6-trifluoromethyl-pyridin-3-ylmethyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl} ester **(363)**,

Phosphoric acid mono-{6-oxo-1-propyl-8-[1-(6-trifluoromethyl-pyridin-3-ylmethyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl} ester **(364)**,

Benzoic acid 2-cyano-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl ester **(365)**,
7-Methoxymethyl-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-6,7-dihydro-1H-purine-2-carbonitrile **(366)**,
Acetic acid 2-cyano-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl ester **(367)**,
(S)-Pyrrolidine-1,2-dicarboxylic acid 1-benzyl ester 2-{2-cyano-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-7-ylmethyl} ester **(368)**,
Butyric acid 2-cyano-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-9-ylmethyl ester **(369)**,
Butyric acid 2-cyclopropyl-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-9-ylmethyl ester **(370)**,
Butyric acid 2-chloro-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-9-ylmethyl ester **(371)**,
Butyric acid 6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-9-ylmethyl ester **(372)**,
Phosphoric acid mono-{2-fluoro-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-9-ylmethyl} ester **(373)**,
Phosphoric acid mono-{6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-9-ylmethyl} ester **(374)**, or
Phosphoric acid mono-{2-cyclopropyl-6-oxo-1-propyl-8-[1-(3-trifluoromethyl-benzyl)-1H-pyrazol-4-yl]-1,6-dihydro-purin-9-ylmethyl} ester **(375)**.