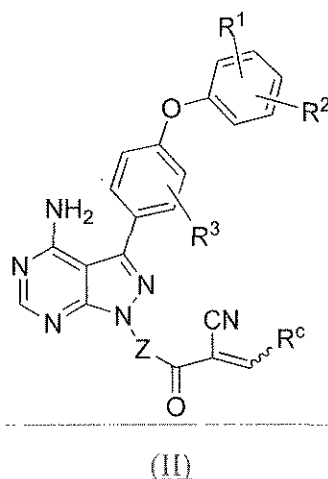


irradiated vascular endothelium. *Cancer Res.* 68:2861-9. 2008) and is also progressively up-regulated during bladder cancer progression (see Guo S., *et al.*, Tyrosine Kinase ETK/BMX Is Up-Regulated in Bladder Cancer and Predicts Poor Prognosis in Patients with Cystectomy. *PLoS One.* 6:e17778. 2011), which can be interpreted to suggest a potential therapeutic target in this type cancer. The B lymphoid kinase (hereafter, sometimes expressed as “BLK”) is reportedly linked through genetic association with a variety of rheumatic diseases including systemic lupus erythematosus and systemic sclerosis (see Ito I, *et al.*, Association of the FAM167A-BLK region with systemic sclerosis. *Arthritis Rheum.* 62:890-5. 2010).

Accordingly, there is a need for compounds that inhibit tyrosine kinases, and particularly BTK inhibitors, thereby providing treatment for diseases such as autoimmune diseases, inflammatory diseases, thromboembolic diseases, and cancer. The present disclosure is directed to such treatment.

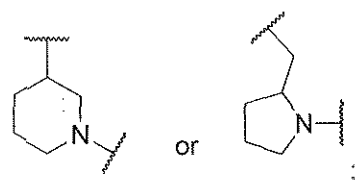
SUMMARY

In one aspect, provided is a compound of Formula (II):



where:

-Z- is:



R¹ and R² are independently hydrogen, alkyl, halo, or alkoxy;

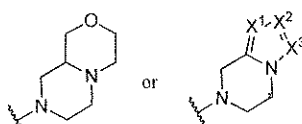
R³ is hydrogen or halo; and

R^c is:

(a) $-\text{C}(\text{CH}_3)_2-(4\text{-R}^5\text{-piperazin-1-yl})$ where R^5 is hydrogen, alkyl, alkoxyalkyl, hydroxyalkyl, haloalkyl, alkylsulfonyl, alkoxycarbonyl, acyl, or oxetan-3-yl and the piperazinyl ring is additionally optionally substituted with one or two alkyl;

(b) $-\text{C}(\text{CH}_3)_2-(2\text{- or }3\text{-oxo-4-R}^a\text{-piperazin-1-yl})$ where R^a is hydrogen, alkyl, cycloalkyl, alkoxyalkyl, haloalkyl, or oxetan-3-yl and the piperazinyl ring is additionally optionally substituted with one or two alkyl;

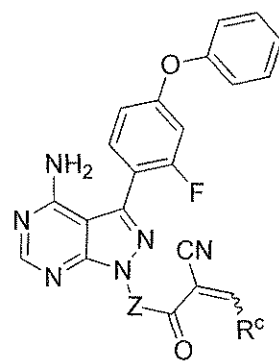
(c) $-\text{C}(\text{CH}_3)_2\text{-NR}^b\text{oxetan-3-yl}$ where R^b is hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, or cycloalkyl;

(d) $-\text{C}(\text{CH}_3)_2\text{-R}^c$ where R^c is  where one or two of X^1 , X^2 and X^3 are nitrogen and the rest are carbon and the ring is optionally substituted with one or two substituents independently selected from alkyl, haloalkyl, or halo; or

(e) $-\text{C}(\text{CH}_3)_2\text{-2-oxa-6-azaspiro[3.3]heptan-6-yl}$, or $-\text{C}(\text{CH}_3)_2\text{-CH}_2\text{morpholine-4-yl}$;

and/or a pharmaceutically acceptable salt thereof.

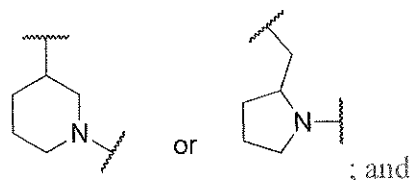
In another aspect, provided is a compound of Formula (IA):



(IA)

where:

$-\text{Z}-$ is:

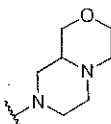
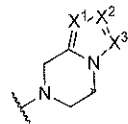


R^c is:

(a) $-\text{C}(\text{CH}_3)_2-(4-\text{R}^4\text{-piperazin-1-yl})$ where R^4 is hydrogen, alkyl, alkoxyalkyl, haloalkyl, alkylsulfonyl, alkoxycarbonyl, acyl, or oxetan-3-yl and the piperazinyl ring is additionally optionally substituted with one or two alkyl;

(b) $-\text{C}(\text{CH}_3)_2-(3\text{-oxo-4-}\text{R}^a\text{-piperazin-1-yl})$ where R^a is hydrogen, alkyl, cycloalkyl, alkoxyalkyl, haloalkyl, or oxetan-3-yl and the piperazinyl ring is additionally optionally substituted with one or two alkyl;

(c) $-\text{C}(\text{CH}_3)_2\text{-NR}^b\text{oxetan-3-yl}$ where R^b is hydrogen, alkyl, alkoxyalkyl, or cycloalkyl;

(d) $-\text{C}(\text{CH}_3)_2\text{-R}^c$ where R^c is  or  where one or two of X^1 , X^2 and X^3 are nitrogen and the rest are carbon and the ring is optionally substituted with one or two substituents independently selected from alkyl, haloalkyl, or halo; or

(e) $-\text{C}(\text{CH}_3)_2\text{-2-oxa-6-azaspiro[3.3]heptan-6-yl}$, or $-\text{C}(\text{CH}_3)_2\text{-CH}_2\text{morpholine-4-yl}$;

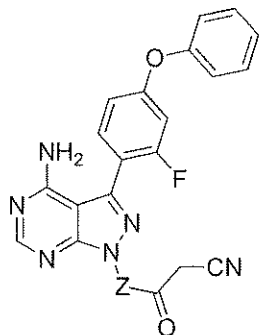
and/or a pharmaceutically acceptable salt thereof.

Another aspect relates to a pharmaceutical composition comprising a compound as disclosed herein and/or a pharmaceutically acceptable salt and a pharmaceutically acceptable excipient.

Yet another aspect relates to the use of a compound as disclosed herein or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of a disease treatable by inhibition of Bruton tyrosine kinase.

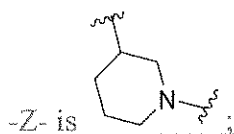
A further aspect relates to a process of preparing a compound as disclosed herein, the method comprising:

(a) reacting a compound of formula (1):



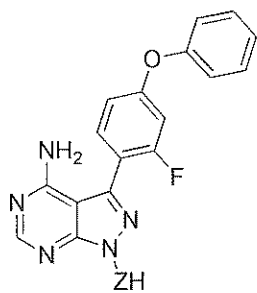
(1)

wherein:



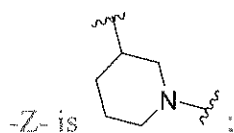
with an aldehyde of formula $R^c\text{CHO}$ where R^c is $-\text{C}(\text{CH}_3)_2\text{-(piperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(4-methylpiperazin-1-yl)}$, or $-\text{C}(\text{CH}_3)_2\text{-4-(oxetan-3-yl)piperazin-1-yl}$; or

5 (b) reacting a compound of formula (2):



(2)

wherein:



10 with a compound of formula $R^c\text{CH}=\text{C}(\text{CN})\text{CO}_2\text{H}$ or $R^c\text{CH}=\text{C}(\text{CN})\text{COX}$ (where R^c is $-\text{C}(\text{CH}_3)_2\text{-(piperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(4-methylpiperazin-1-yl)}$, or $-\text{C}(\text{CH}_3)_2\text{-4-(oxetan-3-yl)piperazin-1-yl}$) and X is a leaving group capable of being displaced by the nitrogen atom of the Z group under amide coupling reaction conditions;

(c) optionally making an acid addition salt of a compound obtained from Steps (a) or

15 (b) above;

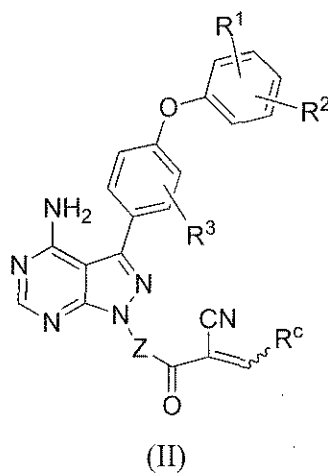
(d) optionally making a free base of a compound obtained from Steps (a), (b), or (c) above;

(e) optionally separating individual stereoisomers of the compounds obtained from Steps (a), (b), (c), or (d) above; and

20 (f) optionally separating individual (E) and (Z) isomers of the compounds obtained from Steps (a), (b), (c), (d), or (e) above.

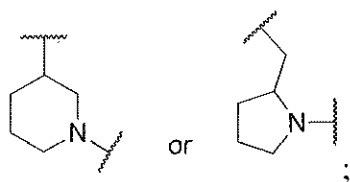
DETAILED DESCRIPTION

In an embodiment, provided is a compound of Formula (II):



where:

-Z- is:



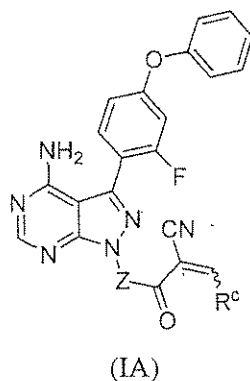
R^1 and R^2 are independently hydrogen, alkyl, halo, or alkoxy;

10 R^3 is hydrogen or halo; and

R^c is:

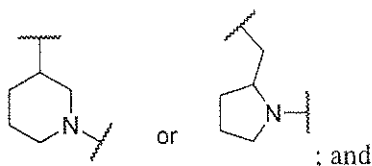
What is Claimed:

1. A compound of Formula (IA):



where:

-Z- is:



R^c is:

(a) $-C(CH_3)_2-(4-R^4\text{-piperazin-1-yl})$ where R^4 is hydrogen, alkyl, alkoxyalkyl, haloalkyl, alkylsulfonyl, alkoxycarbonyl, acyl, or oxetan-3-yl and the piperazinyl ring is additionally optionally substituted with one or two alkyl;

(b) $-C(CH_3)_2-(3\text{-oxo-4-}R^a\text{-piperazin-1-yl})$ where R^a is hydrogen, alkyl, cycloalkyl, alkoxyalkyl, haloalkyl, or oxetan-3-yl and the piperazinyl ring is additionally optionally substituted with one or two alkyl;

(c) $-C(CH_3)_2-NR^b\text{-oxetan-3-yl}$ where R^b is hydrogen, alkyl, alkoxyalkyl, or cycloalkyl;

(d) $-C(CH_3)_2-R^c$ where R^c is where one or two of X^1 , X^2 and X^3 are nitrogen and the rest are carbon and the ring is optionally substituted with one or two substituents independently selected from alkyl, haloalkyl, or halo; or

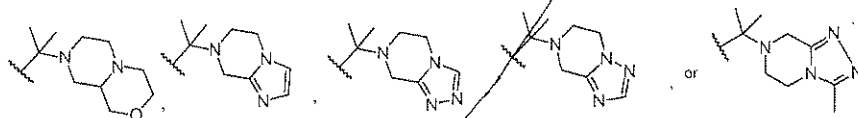
(e) $-C(CH_3)_2\text{-2-oxa-6-azaspiro[3.3]heptan-6-yl}$, or $-C(CH_3)_2\text{-CH}_2\text{morpholine-4-yl}$; or

;

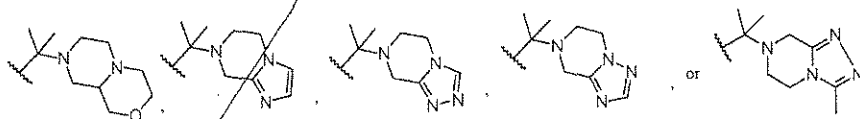
and/or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1 and/or a pharmaceutically acceptable salt thereof wherein R^c is:

- $-\text{C}(\text{CH}_3)_2\text{-(piperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(4-methylpiperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(4-ethylpiperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-N}(\text{CH}_3)\text{oxetan-3-yl}$, $-\text{C}(\text{CH}_3)_2\text{-N}(\text{CH}_2\text{CH}_3)\text{oxetan-3-yl}$,
 5 $\text{C}(\text{CH}_3)_2\text{-N}(\text{cyclopropyl})\text{-oxetan-3-yl}$, $-\text{C}(\text{CH}_3)_2\text{-NHoxetan-3-yl}$, $-\text{C}(\text{CH}_3)_2\text{-2-oxa-6-azaspiro[3.3]heptan-6-yl}$, $-\text{C}(\text{CH}_3)_2\text{-CH}_2\text{morpholine-4-yl}$, $-\text{C}(\text{CH}_3)_2\text{-(4-methylsulfonyl-piperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(3-oxo-4-methylpiperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-[4-(2-methoxyethyl)-piperazin-1-yl]}$, $-\text{C}(\text{CH}_3)_2\text{-(4-tert-butylpiperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(4-acetylpiperazin-1-yl)}$,
 10 $-\text{C}(\text{CH}_3)_2\text{-(4-2,2,2-trifluoroethyl-piperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(4-isopropylpiperazin-1-yl)}$,
 $\text{C}(\text{CH}_3)_2\text{-(2,5-dimethyl-piperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(3,5-dimethylpiperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(3,4,5-trimethylpiperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(2,4,5-trimethylpiperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(4-oxetan-3-ylpiperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(4-methoxycarbonylpiperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(3,5-dimethylpiperazin-1-yl)}$,



- 15 3. The compound of Claim 1 and/or a pharmaceutically acceptable salt thereof wherein R^c is $-\text{C}(\text{CH}_3)_2\text{-(3-oxo-4-methylpiperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-[4-(2-methoxyethyl)-piperazin-1-yl]}$, $-\text{C}(\text{CH}_3)_2\text{-(4-tert-butylpiperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(4-isopropylpiperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(2,5-dimethyl-piperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(3,5-dimethylpiperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(3,4,5-trimethylpiperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(2,4,5-trimethylpiperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(4-oxetan-3-ylpiperazin-1-yl)}$,
 20 $-\text{C}(\text{CH}_3)_2\text{-(4-methoxycarbonylpiperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(3,5-dimethylpiperazin-1-yl)}$, or



4. The compound of Claim 1 and/or a pharmaceutically acceptable salt thereof wherein R^c is $-\text{C}(\text{CH}_3)_2\text{-(piperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(4-methylpiperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(4-ethylpiperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-N}(\text{CH}_3)\text{oxetan-3-yl}$, $-\text{C}(\text{CH}_3)_2\text{-N}(\text{CH}_2\text{CH}_3)\text{oxetan-3-yl}$,
 25 $-\text{C}(\text{CH}_3)_2\text{-N}(\text{cyclopropyl})\text{oxetan-3-yl}$, $-\text{C}(\text{CH}_3)_2\text{-NHoxetan-3-yl}$, or $-\text{C}(\text{CH}_3)_2\text{-2-oxa-6-azaspiro[3.3]heptan-6-yl}$.

5. The compound of Claim 1 and/or a pharmaceutically acceptable salt thereof wherein the compound is chosen from:

2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

5 2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-piperazin-1-yl-pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-piperazin-1-yl-pent-2-enenitrile;

10 2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(oxetan-3-ylamino)pent-2-enenitrile;

15 2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(oxetan-3-ylamino)pent-2-enenitrile;

2-[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

20 2-[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-[[[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

25 2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile;

2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile;

30 (S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(ethyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(ethyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(ethyl(oxetan-3-yl)amino)pent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(ethyl(oxetan-3-yl)amino)pent-2-enenitrile;

5 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

10 (S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

(R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

15 2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

20 2-[[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

2-[[[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(oxetan-3-yl)aminopent-2-enenitrile;

25 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(oxetan-3-yl)aminopent-2-enenitrile;

(R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

30 (S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

5 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-isopropylpiperazin-1-yl)-4-methylpent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-isopropylpiperazin-1-yl)-4-methylpent-2-enenitrile;

10 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-(tert-butyl)piperazin-1-yl)-4-methylpent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-(tert-butyl)piperazin-1-yl)-4-methylpent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-(2-methoxyethyl)piperazin-1-yl)-4-methylpent-2-enenitrile;

15 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-(2-methoxyethyl)piperazin-1-yl)-4-methylpent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile;

20 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((R)-hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-4-methylpent-2-enenitrile;

25 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((R)-hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-4-methylpent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((S)-hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-4-methylpent-2-enenitrile;

30 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((S)-hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-4-methylpent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(2,2,2-trifluoroethyl)piperazin-1-yl)pent-2-enenitrile;

5 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(2,2,2-trifluoroethyl)piperazin-1-yl)pent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((3S,5R)-3,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;

10 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((3S,5R)-3,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((3S,5R)-3,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;

15 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((3S,5R)-3,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((2R,5S)-2,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;

20 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((2R,5S)-2,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((2R,5S)-2,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;

25 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((2R,5S)-2,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((2S,5R)-2,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;

30 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((2S,5R)-2,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((2S,5R)-2,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;

2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((2S,5R)-2,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)-4-methylpent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)-4-methylpent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(methylsulfonyl)piperazin-1-yl)pent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(methylsulfonyl)piperazin-1-yl)pent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-methyl-3-oxopiperazin-1-yl)pent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-methyl-3-oxopiperazin-1-yl)pent-2-enenitrile;

(R)-4-(4-acetylpiperazin-1-yl)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methylpent-2-enenitrile;

(S)-4-(4-acetylpiperazin-1-yl)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methylpent-2-enenitrile;

(R)-methyl 4-(5-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)-4-cyano-2-methyl-5-oxopent-3-en-2-yl)piperazine-1-carboxylate;

(S)-methyl 4-(5-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)-4-cyano-2-methyl-5-oxopent-3-en-2-yl)piperazine-1-carboxylate;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4,4-dimethyl-5-morpholinopent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4,4-dimethyl-5-morpholinopent-2-enenitrile;

or a mixture of R and S isomers thereof; or

an (E) or (Z) isomer of any of the above compounds.

6. An E isomer of any of:

2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

5 2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-piperazin-1-yl-pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-piperazin-1-yl-pent-2-enenitrile;

10 2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

15 2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(oxetan-3-ylamino)pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(oxetan-3-ylamino)pent-2-enenitrile;

2-[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

20 2-[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

25 2-[[[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile;

2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile;

30 (S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(ethyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(ethyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(ethyl(oxetan-3-yl)amino)pent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(ethyl(oxetan-3-yl)amino)pent-2-enenitrile;

5 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

10 (S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

(R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

15 2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

20 2-[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

2-[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(oxetan-3-yl)aminopent-2-enenitrile;

25 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(oxetan-3-yl)aminopent-2-enenitrile;

(R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

30 (S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

5 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-isopropylpiperazin-1-yl)-4-methylpent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-isopropylpiperazin-1-yl)-4-methylpent-2-enenitrile;

10 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-(tert-butyl)piperazin-1-yl)-4-methylpent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-(tert-butyl)piperazin-1-yl)-4-methylpent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-(2-methoxyethyl)piperazin-1-yl)-4-methylpent-2-enenitrile;

15 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-(2-methoxyethyl)piperazin-1-yl)-4-methylpent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile;

20 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((R)-hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-4-methylpent-2-enenitrile;

25 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((R)-hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-4-methylpent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((S)-hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-4-methylpent-2-enenitrile;

30 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((S)-hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-4-methylpent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(2,2,2-trifluoroethyl)piperazin-1-yl)pent-2-enenitrile;

5 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(2,2,2-trifluoroethyl)piperazin-1-yl)pent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((3S,5R)-3,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;

10 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((3S,5R)-3,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((3S,5R)-3,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;

15 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((3S,5R)-3,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((2R,5S)-2,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;

20 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((2R,5S)-2,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((2R,5S)-2,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;

25 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((2R,5S)-2,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((2S,5R)-2,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;

30 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((2S,5R)-2,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((2S,5R)-2,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;

2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((2S,5R)-2,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;

5 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)-4-methylpent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)-4-methylpent-2-enenitrile;

10 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(methylsulfonyl)piperazin-1-yl)pent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(methylsulfonyl)piperazin-1-yl)pent-2-enenitrile;

15 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-methyl-3-oxopiperazin-1-yl)pent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-methyl-3-oxopiperazin-1-yl)pent-2-enenitrile;

(R)-4-(4-acetylpiperazin-1-yl)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methylpent-2-enenitrile;

20 (S)-4-(4-acetylpiperazin-1-yl)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methylpent-2-enenitrile;

(R)-methyl 4-(5-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)-4-cyano-2-methyl-5-oxopent-3-en-2-yl)piperazine-1-carboxylate;

25 (S)-methyl 4-(5-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)-4-cyano-2-methyl-5-oxopent-3-en-2-yl)piperazine-1-carboxylate;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4,4-dimethyl-5-morpholinopent-2-enenitrile;

30 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4,4-dimethyl-5-morpholinopent-2-enenitrile;

and/or of any pharmaceutically acceptable salt thereof.

7. A Z isomer of any of:

2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

5 2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-piperazin-1-yl-pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-piperazin-1-yl-pent-2-enenitrile;

10 2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(oxetan-3-ylamino)pent-2-enenitrile;

15 2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(oxetan-3-ylamino)pent-2-enenitrile;

2-[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

20 2-[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-[[[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

25 2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile;

2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile;

30 (S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(ethyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(ethyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(ethyl(oxetan-3-yl)amino)pent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(ethyl(oxetan-3-yl)amino)pent-2-enenitrile;

5 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

10 (S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

(R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

15 2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

20 2-[[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

2-[[[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(oxetan-3-yl)aminopent-2-enenitrile;

25 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(oxetan-3-yl)aminopent-2-enenitrile;

(R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

30 (S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

5 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-isopropylpiperazin-1-yl)-4-methylpent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-isopropylpiperazin-1-yl)-4-methylpent-2-enenitrile;

10 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-(tert-butyl)piperazin-1-yl)-4-methylpent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-(tert-butyl)piperazin-1-yl)-4-methylpent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-(2-methoxyethyl)piperazin-1-yl)-4-methylpent-2-enenitrile;

15 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-(2-methoxyethyl)piperazin-1-yl)-4-methylpent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile;

20 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((R)-hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-4-methylpent-2-enenitrile;

25 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((R)-hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-4-methylpent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((S)-hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-4-methylpent-2-enenitrile;

30 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((S)-hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-4-methylpent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(2,2,2-trifluoroethyl)piperazin-1-yl)pent-2-enenitrile;

5 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(2,2,2-trifluoroethyl)piperazin-1-yl)pent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((3S,5R)-3,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;

10 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((3S,5R)-3,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((3S,5R)-3,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;

15 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((3S,5R)-3,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((2R,5S)-2,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;

20 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((2R,5S)-2,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((2R,5S)-2,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;

25 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((2R,5S)-2,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((2S,5R)-2,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;

30 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((2S,5R)-2,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((2S,5R)-2,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;

2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((2S,5R)-2,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;

5 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)-4-methylpent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)-4-methylpent-2-enenitrile;

10 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(methylsulfonyl)piperazin-1-yl)pent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(methylsulfonyl)piperazin-1-yl)pent-2-enenitrile;

15 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-methyl-3-oxopiperazin-1-yl)pent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-methyl-3-oxopiperazin-1-yl)pent-2-enenitrile;

(R)-4-(4-acetylpiperazin-1-yl)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methylpent-2-enenitrile;

20 (S)-4-(4-acetylpiperazin-1-yl)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methylpent-2-enenitrile;

(R)-methyl 4-(5-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)-4-cyano-2-methyl-5-oxopent-3-en-2-yl)piperazine-1-carboxylate;

25 (S)-methyl 4-(5-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)-4-cyano-2-methyl-5-oxopent-3-en-2-yl)piperazine-1-carboxylate;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4,4-dimethyl-5-morpholinopent-2-enenitrile;

30 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4,4-dimethyl-5-morpholinopent-2-enenitrile;

and/or of any pharmaceutically acceptable salt thereof.

8. The compound of Claim 5 and/or a pharmaceutically acceptable salt thereof wherein the compound is chosen from:

2-[(2RS)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

5 2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

10 2-[(2RS)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-piperazin-1-yl-pent-2-enenitrile;

2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-piperazin-1-yl-pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-piperazin-1-yl-pent-2-enenitrile;

15 2-[(2RS)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

20 2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[(2RS)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(oxetan-3-ylamino)pent-2-enenitrile;

2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(oxetan-3-ylamino)pent-2-enenitrile;

25 2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(oxetan-3-ylamino)pent-2-enenitrile;

2-[(3RS)-3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

30 2-[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[[[(3RS)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-[[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

5 2-[[[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-((RS)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile;

10 2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile;

2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile;

(RS)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(ethyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

15 (S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(ethyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(ethyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

20 (RS)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(ethyl(oxetan-3-yl)amino)pent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(ethyl(oxetan-3-yl)amino)pent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(ethyl(oxetan-3-yl)amino)pent-2-enenitrile;

25 (RS)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

30 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

(RS)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

(S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

(R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

2-[(2RS)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

2-[(3RS)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

2-[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

2-[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

(RS)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(oxetan-3-yl)aminopent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(oxetan-3-yl)aminopent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(oxetan-3-yl)aminopent-2-enenitrile;

(RS)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(RS)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

- 5 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile; or
an (E) or (Z) isomer of any of the above compounds.

9. An E isomer of any of:

- 2-[(2RS)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-
10 methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-
methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-
methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

- 15 2-[(2RS)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-
yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-piperazin-1-yl-pent-2-enenitrile;

2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-
yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-piperazin-1-yl-pent-2-enenitrile;

- 20 2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-
yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-piperazin-1-yl-pent-2-enenitrile;

2-[(2RS)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-
yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-
yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

- 25 2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-
yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[(2RS)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-
yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(oxetan-3-ylamino)pent-2-enenitrile;

- 30 2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-
yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(oxetan-3-ylamino)pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-
yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(oxetan-3-ylamino)pent-2-enenitrile;

2-[(3RS)-3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

5 2-[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[[(3RS)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

10 2-[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-[[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-((RS)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile;

15 2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile;

2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile;

20 (RS)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(ethyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(ethyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(ethyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

25 (RS)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(ethyl(oxetan-3-yl)amino)pent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(ethyl(oxetan-3-yl)amino)pent-2-enenitrile;

30 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(ethyl(oxetan-3-yl)amino)pent-2-enenitrile;

(RS)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

- (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;
- (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;
- 5 (RS)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;
- (S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-
- 10 enenitrile;
- (R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;
- 2-[(2RS)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;
- 15 2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;
- 2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;
- 20 2-[[[(3RS)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;
- 2-[[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;
- 2-[[[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;
- 25 (RS)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(oxetan-3-yl)aminopent-2-enenitrile;
- (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(oxetan-3-yl)aminopent-2-enenitrile;
- 30 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(oxetan-3-yl)aminopent-2-enenitrile;

(RS)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(RS)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

and/or a pharmaceutically acceptable salt of any of the foregoing.

10. A Z isomer of any of:

2-[(2RS)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-[(2RS)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-piperazin-1-yl-pent-2-enenitrile;

2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-piperazin-1-yl-pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-piperazin-1-yl-pent-2-enenitrile;

2-[(2RS)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl)methyl]pyrrolidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[(2RS)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl)methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(oxetan-3-ylamino)pent-2-enenitrile;

5 2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl)methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(oxetan-3-ylamino)pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl)methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(oxetan-3-ylamino)pent-2-enenitrile;

10 2-[(3RS)-3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

2-[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

15 2-[[[(3RS)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-[[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

20 2-[[[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-((RS)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile;

2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile;

25 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile;

(RS)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(ethyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

30 (S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(ethyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(ethyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(RS)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(ethyl(oxetan-3-yl)amino)pent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(ethyl(oxetan-3-yl)amino)pent-2-enenitrile;

5 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(ethyl(oxetan-3-yl)amino)pent-2-enenitrile;

(RS)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

10 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

15 (RS)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

(S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

20 (R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

2-[(2RS)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

25 2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

2-[(3RS)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

30 2-[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

2-[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

(RS)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(oxetan-3-yl)aminopent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(oxetan-3-yl)aminopent-2-enenitrile;

5 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(oxetan-3-yl)aminopent-2-enenitrile;

(RS)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

10 (R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

15 (RS)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

20 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;
and/or a pharmaceutically acceptable salt of any of the foregoing.

11. A compound chosen from 2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-
25 [methyl(oxetan-3-yl)amino]pent-2-enenitrile, or an (E) or (Z) isomer thereof, and/or a pharmaceutically acceptable salt of any of the foregoing compounds.

12. An E isomer of 2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile and/or a pharmaceutically acceptable salt thereof.

30 13. A Z isomer of 2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile and/or a pharmaceutically acceptable salt thereof.

14. A compound chosen from 2-[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile, or an (E) or (Z) isomer thereof, and/or a pharmaceutically acceptable salt of any of the foregoing compounds.

5 15. An E isomer of 2-[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile and/or a pharmaceutically acceptable salt thereof.

16. A Z isomer of 2-[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-
10 enenitrile and/or a pharmaceutically acceptable salt thereof.

17. A compound chosen from 2-[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile, or an (E) or (Z) isomer, and/or a pharmaceutically acceptable salt of any of the foregoing compounds.

15 18. An E isomer of 2-[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile and/or a pharmaceutically acceptable salt thereof.

19. A Z isomer of 2-[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-
20 enenitrile and/or a pharmaceutically acceptable salt thereof. 20. A compound chosen from 2-[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile, or an (E) or (Z) isomer, and/or a pharmaceutically acceptable salt of any of the foregoing compounds.

21. An E isomer of 2-[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile
25 and/or a pharmaceutically acceptable salt thereof.

22. A Z isomer of 2-[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile
and/or a pharmaceutically acceptable salt thereof.

30

23. A compound chosen from (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-

1-yl)pent-2-enenitrile; or an (E) or (Z) isomer, and/or a pharmaceutically acceptable salt of any of the foregoing compounds.

24. An E isomer of (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile and/or a pharmaceutically acceptable salt thereof.

25. A Z isomer of (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile and/or a pharmaceutically acceptable salt thereof.

26. A compound chosen from (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile and/or a pharmaceutically acceptable salt of any of the foregoing compounds.

27. A compound chosen from 2-[[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile and/or a pharmaceutically acceptable salt of any of the foregoing compounds.

28. A compound chosen from 2-[[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile and/or a pharmaceutically acceptable salt of any of the foregoing compounds.

29. A pharmaceutical composition comprising a compound and/or a pharmaceutically acceptable salt of any one of Claims 1 to 28 of any of the foregoing compounds, and a pharmaceutically acceptable excipient.

30. A method of treating a disease treatable by inhibition of a tyrosine kinase in a patient which method comprises administering to the patient in recognized need of such treatment, a pharmaceutical composition comprising a compound, or an (E) or (Z) isomer thereof, and/or pharmaceutically acceptable salt of any of Claims 1 to 28 and a pharmaceutically acceptable excipient in a therapeutically effective amount.

31. The method of claim 30 wherein the tyrosine kinase is BTK.

32. The method of Claim 31 wherein the disease is chosen from autoimmune diseases, inflammatory diseases, and cancers.

33. The method of Claim 31 wherein the disease is chosen from rheumatoid arthritis, psoriatic arthritis, lupus, uveitis, myasthenia gravis, warm autoimmune hemolytic anemia,

Wegener's granulomatosis, Sjogren's disease, Sjogren's dry eye, non-Sjogren's dry eye disease, psoriasis, and asthma.

34. The method of Claim 31 wherein the disease is chosen from B-cell proliferative disorders.

5 35. The method of Claim 34 wherein the proliferative disorders are chosen from diffuse large B cell lymphoma, follicular lymphoma, chronic lymphocytic lymphoma, chronic lymphocytic leukemia, B-cell prolymphocytic leukemia, small lymphocytic lymphoma (SLL), multiple myeloma, B-cell non-Hodgkin lymphoma, lymphoplasmacytic lymphoma/Waldenstrom macroglobulinemia, splenic marginal zone lymphoma, plasma cell
10 myeloma, plasmacytoma, extranodal marginal zone B cell lymphoma, nodal marginal zone B cell lymphoma, mantle cell lymphoma, mediastinal (thymic) large B cell lymphoma, intravascular large B cell lymphoma, primary effusion lymphoma, burkitt lymphoma/leukemia, and lymphomatoid granulomatosis.

36. The method of Claim 34 or 35 wherein the compound and/or pharmaceutically
15 acceptable salt is administered in combination with one or more anti-cancer or anti-inflammatory agents.

37. The compound of any one of Claims 1 to 28 or a pharmaceutically acceptable salt thereof for use in the treatment of a disease mediated by a tyrosine kinase.

38. The use of Claim 37 wherein the tyrosine kinase is BTK.

20 39. The use of Claim 38 wherein the disease is chosen from autoimmune diseases, inflammatory diseases, and cancers.

40. The use of Claim 39 wherein the disease is chosen from rheumatoid arthritis, psoriatic arthritis, lupus, uveitis, myasthenia gravis, warm autoimmune hemolytic anemia, Wegener's granulomatosis, Sjogren's disease, Sjogren's dry eye, non-Sjogren's dry eye disease,
25 psoriasis, and asthma.

41. The use of Claim 38 wherein the disease is chosen from B-cell proliferative disorders.

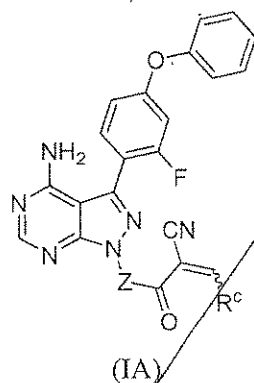
42. The use of Claim 41 wherein the proliferative disorders are chosen from diffuse large B cell lymphoma, follicular lymphoma, chronic lymphocytic lymphoma, chronic lymphocytic leukemia, B-cell prolymphocytic leukemia, small lymphocytic lymphoma (SLL), multiple
30 myeloma, B-cell non-Hodgkin lymphoma, lymphoplasmacytic lymphoma/Waldenstrom macroglobulinemia, splenic marginal zone lymphoma, plasma cell myeloma, plasmacytoma, extranodal marginal zone B cell lymphoma, nodal marginal zone B cell lymphoma, mantle cell lymphoma, mediastinal (thymic) large B cell lymphoma, intravascular large B cell

lymphoma, primary effusion lymphoma, burkitt lymphoma/leukemia, and lymphomatoid granulomatosis.

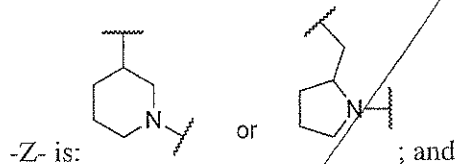
43. The use of claim 41 or 42 wherein the compound or pharmaceutically acceptable salt is administered in combination with one or more anti-cancer or anti-inflammatory agents.

5 44. The compound of any one of Claims 1 to 28 or a pharmaceutically acceptable salt thereof for use as a medicament.

45. A process of preparing a compound of Formula (IA):



10 where:



R^c is:

(a) $-\text{C}(\text{CH}_3)_2-(4\text{-R}^4\text{-piperazin-1-yl})$ where R⁴ is hydrogen, alkyl, alkoxyalkyl, haloalkyl, alkylsulfonyl, alkoxycarbonyl, acyl, or oxetan-3-yl and the piperazinyl ring is additionally optionally substituted with one or two alkyl;

15

(b) $-\text{C}(\text{CH}_3)_2-(3\text{-oxo-4-R}^a\text{-piperazin-1-yl})$ where R^a is hydrogen, alkyl, alkoxyalkyl, haloalkyl, or oxetan-3-yl and the piperazinyl ring is additionally optionally substituted with one or two alkyl;

(c) $-\text{C}(\text{CH}_3)_2\text{-NR}^b\text{-oxetan-3-yl}$ where R^b is hydrogen, alkyl, or cycloalkyl;

(d) $-\text{C}(\text{CH}_3)_2\text{-R}^c$ where R^c is or where one or two of X¹, X² and X³ are nitrogen and the rest are carbon and the ring is optionally substituted with one or two substituents independently selected from alkyl, haloalkyl, or halo; or

20

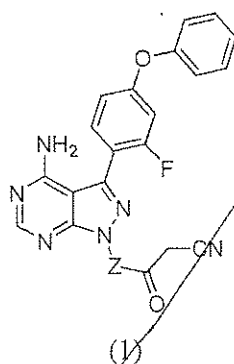
(e) $-\text{C}(\text{CH}_3)_2$ -2-oxa-6-azaspiro[3.3]heptan-6-yl, or $-\text{C}(\text{CH}_3)_2$ -CH₂morpholine-4-yl; ((in one embodiment R^c is $-\text{C}(\text{CH}_3)_2$ -(piperazin-1-yl), $-\text{C}(\text{CH}_3)_2$ -(4-methylpiperazin-1-yl), $-\text{C}(\text{CH}_3)_2$ -(4-ethylpiperazin-1-yl), $-\text{C}(\text{CH}_3)_2$ -N(CH₃)oxetan-3-yl, $-\text{C}(\text{CH}_3)_2$ -N(CH₂CH₃)oxetan-3-yl, $-\text{C}(\text{CH}_3)_2$ -NHoxetan-3-yl, or $-\text{C}(\text{CH}_3)_2$ -2-oxa-6-

5 azaspiro[3.3]heptan-6-yl); and/or

a pharmaceutically salt thereof;

comprising:

(a) reacting a compound of formula (1):



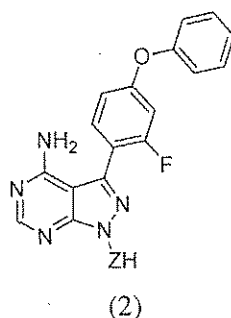
10

where:

-Z- is as defined above;

with an aldehyde of formula R^cCHO where R^c is as defined above; or

(b) reacting a compound of formula (2):



15

where:

-Z- is as defined above;

with a compound of formula R^cCH=C(CN)CO₂H or R^cCH=C(CN)COX (where R^c is as defined above and X is a leaving group capable of being displaced by the nitrogen atom of the Z group under amide coupling reaction conditions;

20

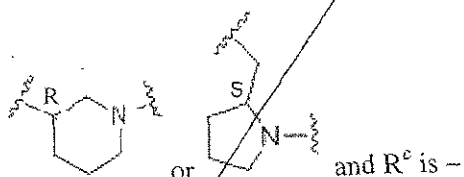
(c) optionally making an acid addition salt of a compound obtained from Steps (a) or (b) above;

(d) optionally making a free base of a compound obtained from Steps (a), (b), or (c) above;

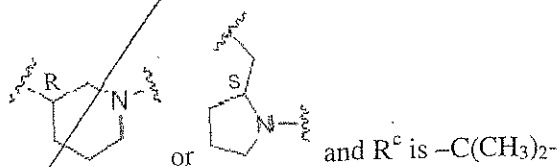
(e) optionally separating individual stereoisomers of the compounds obtained from Steps (a), (b), (c), or (d) above; and

5 (f) optionally separating individual (E) and (Z) isomers of the compounds obtained from Steps (a), (b), (c), (d), or (e) above.

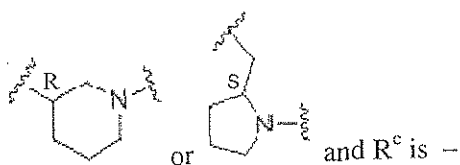
46. The process of Claim 45 wherein Z is $C(CH_3)_2$ -(4-methylpiperazin-1-yl).



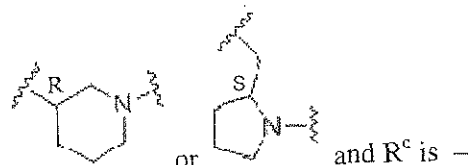
47. The process of Claim 45 wherein Z is (piperazin-1-yl).



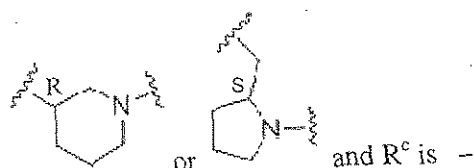
48. The process of Claim 45 wherein Z is $C(CH_3)_2$ -N(CH₃)oxetan-3-yl.



49. The process of Claim 45 wherein Z is $C(CH_3)_2$ -N(ethyl)piperazin-1-yl.

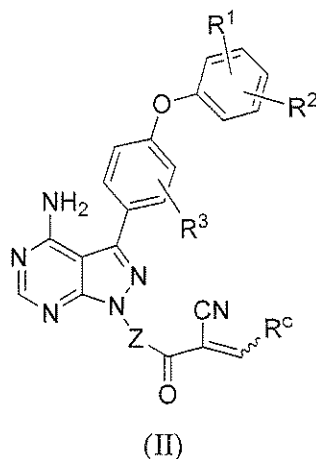


50. The process of Claim 45 wherein Z is $C(CH_3)_2$ -4-(oxetan-3-yl)-piperazin-1-yl.



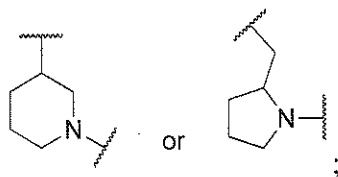
What is claimed is:

1. A compound of Formula (II):



where:

-Z- is:



R^1 and R^2 are independently hydrogen, alkyl, halo, or alkoxy;

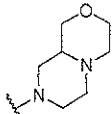
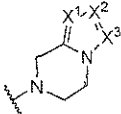
R^3 is hydrogen or halo; and

R^c is:

(a) $-C(CH_3)_2-(4-R^5\text{-piperazin-1-yl})$ where R^5 is hydrogen, alkyl, alkoxyalkyl, hydroxyalkyl, haloalkyl, alkylsulfonyl, alkoxycarbonyl, acyl, or oxetan-3-yl and the piperazinyl ring is additionally optionally substituted with one or two alkyl;

(b) $-C(CH_3)_2-(2\text{- or }3\text{-oxo-4-}R^a\text{-piperazin-1-yl})$ where R^a is hydrogen, alkyl, cycloalkyl, alkoxyalkyl, haloalkyl, or oxetan-3-yl and the piperazinyl ring is additionally optionally substituted with one or two alkyl;

(c) $-C(CH_3)_2-NR^b\text{oxetan-3-yl}$ where R^b is hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, or cycloalkyl;

(d) $-\text{C}(\text{CH}_3)_2\text{-R}^d$ where R^d is  or  where one or two of X^1 , X^2 and

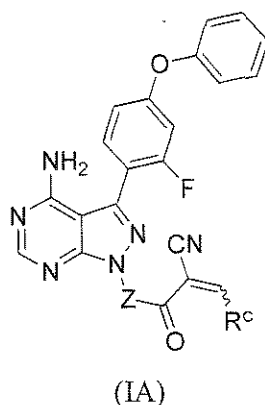
X^3 are nitrogen and the rest are carbon and the ring is optionally substituted with one or two substituents independently selected from alkyl, haloalkyl, or halo; or

(e) $-\text{C}(\text{CH}_3)_2\text{-2-oxa-6-azaspiro[3.3]heptan-6-yl}$, or $-\text{C}(\text{CH}_3)_2\text{-CH}_2\text{morpholine-4-yl}$;
 5 and/or a pharmaceutically acceptable salt thereof.

2. The compound of Claim 1 or a pharmaceutically acceptable salt thereof wherein R^1 and R^2 are hydrogen and R^c is $-\text{C}(\text{CH}_3)_2\text{-(4-R}^5\text{-piperazin-1-yl)}$ where R^5 is hydrogen, alkyl, alkoxyalkyl, hydroxyalkyl, haloalkyl, alkylsulfonyl, alkoxycarbonyl, acyl, or oxetan-3-yl and the
 10 piperazinyl ring is additionally optionally substituted with one or two alkyl.

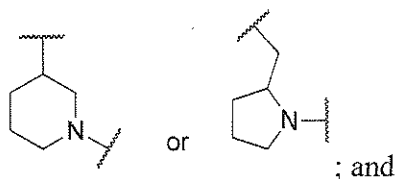
3 The compound of Claim 1 or a pharmaceutically acceptable salt thereof wherein R^1 is hydrogen, alkyl, halo, or alkoxy and R^2 is alkyl, halo, or alkoxy and R^c is $-\text{C}(\text{CH}_3)_2\text{-(4-R}^5\text{-piperazin-1-yl)}$ where R^5 is hydrogen, alkyl, alkoxyalkyl, hydroxyalkyl, haloalkyl, alkylsulfonyl,
 15 alkoxycarbonyl, acyl, or oxetan-3-yl and the piperazinyl ring is additionally optionally substituted with one or two alkyl.

4. A compound of Formula (IA):



where:

-Z- is:



R^c is:

(a) $-C(CH_3)_2-(4-R^4\text{-piperazin-1-yl})$ where R^4 is hydrogen, alkyl, alkoxyalkyl, haloalkyl, alkylsulfonyl, alkoxycarbonyl, acyl, or oxetan-3-yl and the piperazinyl ring is additionally optionally substituted with one or two alkyl;

(b) $-C(CH_3)_2-(3\text{-oxo-4-}R^a\text{-piperazin-1-yl})$ where R^a is hydrogen, alkyl, cycloalkyl, alkoxyalkyl, haloalkyl, or oxetan-3-yl and the piperazinyl ring is additionally optionally substituted with one or two alkyl;

(c) $-C(CH_3)_2-NR^b\text{oxetan-3-yl}$ where R^b is hydrogen, alkyl, alkoxyalkyl, or cycloalkyl;

(d) $-C(CH_3)_2-R^d$ where R^d is where one or two of X^1 , X^2 and

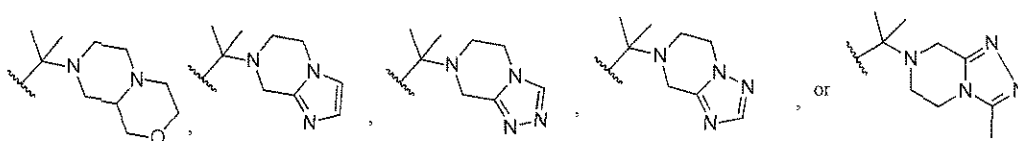
X^3 are nitrogen and the rest are carbon and the ring is optionally substituted with one or two substituents independently selected from alkyl, haloalkyl, or halo; or

(e) $-C(CH_3)_2\text{-2-oxa-6-azaspiro[3.3]heptan-6-yl}$, or $-C(CH_3)_2\text{-CH}_2\text{morpholine-4-yl}$; and/or a pharmaceutically acceptable salt thereof.

5. The compound of claim 4 and/or a pharmaceutically acceptable salt thereof wherein R^c is:

$-C(CH_3)_2\text{-(piperazin-1-yl)}$, $-C(CH_3)_2\text{-(4-methylpiperazin-1-yl)}$,
 $-C(CH_3)_2\text{-(4-ethylpiperazin-1-yl)}$, $-C(CH_3)_2\text{-N(CH}_3\text{)oxetan-3-yl}$,
 $-C(CH_3)_2\text{-N(CH}_2\text{CH}_3\text{)oxetan-3-yl}$, $-C(CH_3)_2\text{-N(cyclopropyl)-oxetan-3-yl}$,
 $-C(CH_3)_2\text{-NHoxetan-3-yl}$, $-C(CH_3)_2\text{-2-oxa-6-azaspiro[3.3]heptan-6-yl}$, $-C(CH_3)_2\text{-CH}_2\text{morpholine-4-yl}$,
 $-C(CH_3)_2\text{-(4-methylsulfonyl-piperazin-1-yl)}$, $-C(CH_3)_2\text{-(3-oxo-4-methylpiperazin-1-yl)}$,
 $-C(CH_3)_2\text{-[4-(2-methoxyethyl)-piperazin-1-yl]}$, $-C(CH_3)_2\text{-(4-tert-butylpiperazin-1-yl)}$,
 $-C(CH_3)_2\text{-(4-acetyl-piperazin-1-yl)}$,
 $-C(CH_3)_2\text{-(4-2,2,2-trifluoroethyl-piperazin-1-yl)}$,

$-\text{C}(\text{CH}_3)_2-(4\text{-isopropylpiperazin-1-yl})$,
 $-\text{C}(\text{CH}_3)_2-(2,5\text{-dimethyl-piperazin-1-yl})$,
 $-\text{C}(\text{CH}_3)_2-(3,5\text{-dimethylpiperazin-1-yl})$,
 $-\text{C}(\text{CH}_3)_2-(3,4,5\text{-trimethylpiperazin-1-yl})$,
 $-\text{C}(\text{CH}_3)_2-(2,4,5\text{-trimethylpiperazin-1-yl})$,
 $-\text{C}(\text{CH}_3)_2-(4\text{-oxetan-3-ylpiperazin-1-yl})$,
 $-\text{C}(\text{CH}_3)_2-(4\text{-methoxycarbonylpiperazin-1-yl})$,
 $-\text{C}(\text{CH}_3)_2-(3,5\text{-dimethylpiperazin-1-yl})$,



6. The compound of Claim 4 and/or a pharmaceutically acceptable salt thereof wherein R^c is $-\text{C}(\text{CH}_3)_2-(\text{piperazin-1-yl})$, $-\text{C}(\text{CH}_3)_2-(4\text{-methylpiperazin-1-yl})$, $-\text{C}(\text{CH}_3)_2-(4\text{-ethyl-piperazin-1-yl})$, $-\text{C}(\text{CH}_3)_2-\text{N}(\text{CH}_3)\text{oxetan-3-yl}$, $-\text{C}(\text{CH}_3)_2-\text{N}(\text{CH}_2\text{CH}_3)\text{oxetan-3-yl}$,
 15 $-\text{C}(\text{CH}_3)_2-\text{N}(\text{cyclopropyl})\text{oxetan-3-yl}$, $-\text{C}(\text{CH}_3)_2-\text{NHoxetan-3-yl}$, or $-\text{C}(\text{CH}_3)_2\text{-2-oxa-6-azaspiro[3.3]heptan-6-yl}$.

7. The compound of Claim 4 and/or a pharmaceutically acceptable salt thereof wherein the compound is chosen from:

20 2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

25 2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-piperazin-1-yl-pent-2-enenitrile;

2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-piperazin-1-yl-pent-2-enenitrile;

2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;

- 2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;
- 2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(oxetan-3-ylamino)pent-2-enenitrile;
- 5 2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(oxetan-3-ylamino)pent-2-enenitrile;
- 2-[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;
- 2-[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[methyl(oxetan-3-yl)amino]pent-2-enenitrile;
- 10 2-[[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;
- 2-[[[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;
- 15 2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile;
- 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile;
- (S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(ethyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;
- 20 (R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(ethyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;
- (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(ethyl(oxetan-3-yl)amino)pent-2-enenitrile;
- 25 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(ethyl(oxetan-3-yl)amino)pent-2-enenitrile;
- (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;
- (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;
- 30

(S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

5 (R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-methyl-4-(2-oxa-6-azaspiro[3.3]heptan-6-yl)pent-2-enenitrile;

2-[(2S)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

10 2-[(2R)-2-[[4-amino-3-(2-fluoro-4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]-methyl]pyrrolidine-1-carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

2-[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

2-[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-ethylpiperazin-1-yl)pent-2-enenitrile;

15 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(oxetan-3-yl)aminopent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(oxetan-3-yl)aminopent-2-enenitrile;

20 (R)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(S)-2-(2-((4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)pyrrolidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

25 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(cyclopropyl(oxetan-3-yl)amino)-4-methylpent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-isopropylpiperazin-1-yl)-4-methylpent-2-enenitrile;

30 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-isopropylpiperazin-1-yl)-4-methylpent-2-enenitrile;

- (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-(tert-butyl)piperazin-1-yl)-4-methylpent-2-enenitrile;
- (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-(tert-butyl)piperazin-1-yl)-4-methylpent-2-enenitrile;
- 5 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-(2-methoxyethyl)piperazin-1-yl)-4-methylpent-2-enenitrile;
- (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(4-(2-methoxyethyl)piperazin-1-yl)-4-methylpent-2-enenitrile;
- (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile;
- 10 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile;
- 2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((R)-hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-4-methylpent-
- 15 2-enenitrile;
- 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((R)-hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-4-methylpent-
- 2-enenitrile;
- 2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((S)-hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-4-methylpent-
- 20 2-enenitrile;
- 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((S)-hexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-4-methylpent-
- 2-enenitrile;
- 25 (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(2,2,2-trifluoroethyl)piperazin-1-yl)pent-2-enenitrile;
- (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(2,2,2-trifluoroethyl)piperazin-1-yl)pent-2-enenitrile;
- 2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((3S,5R)-3,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;
- 30

- 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((3S,5R)-3,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;
- 2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((3S,5R)-3,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;
- 5 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((3S,5R)-3,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;
- 2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((2R,5S)-2,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;
- 10 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((2R,5S)-2,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;
- 2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((2R,5S)-2,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;
- 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((2R,5S)-2,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;
- 15 2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((2S,5R)-2,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;
- 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-((2S,5R)-2,5-dimethylpiperazin-1-yl)-4-methylpent-2-enenitrile;
- 20 2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((2S,5R)-2,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;
- 2-((S)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-((2S,5R)-2,4,5-trimethylpiperazin-1-yl)pent-2-enenitrile;
- (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)-4-methylpent-2-enenitrile;
- 25 enenitrile;
- (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-(5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)-4-methylpent-2-enenitrile;
- (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(methylsulfonyl)piperazin-1-yl)pent-2-enenitrile;
- 30

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(methylsulfonyl)piperazin-1-yl)pent-2-enenitrile;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-methyl-3-oxopiperazin-1-yl)pent-2-enenitrile;

5 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-methyl-3-oxopiperazin-1-yl)pent-2-enenitrile;

(R)-4-(4-acetylpiperazin-1-yl)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methylpent-2-enenitrile;

10 (S)-4-(4-acetylpiperazin-1-yl)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methylpent-2-enenitrile;

(R)-methyl 4-(5-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)-4-cyano-2-methyl-5-oxopent-3-en-2-yl)piperazine-1-carboxylate;

15 (S)-methyl 4-(5-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)-4-cyano-2-methyl-5-oxopent-3-en-2-yl)piperazine-1-carboxylate;

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4,4-dimethyl-5-morpholinopent-2-enenitrile;

20 (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4,4-dimethyl-5-morpholinopent-2-enenitrile;

or a mixture of R and S isomers thereof; or

an (E) or (Z) isomer of any one of the above compounds.

8. The compound of Claim 7 and/or a pharmaceutically acceptable salt thereof wherein the
25 compound is:

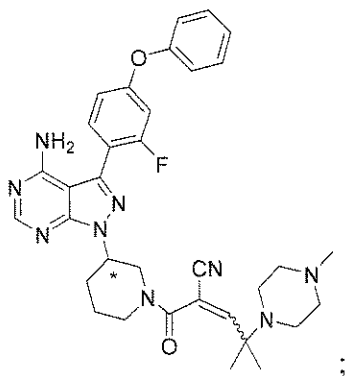
2-[[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-[[[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile; or

30 a mixture of 2-[[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile

and 2-[[[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

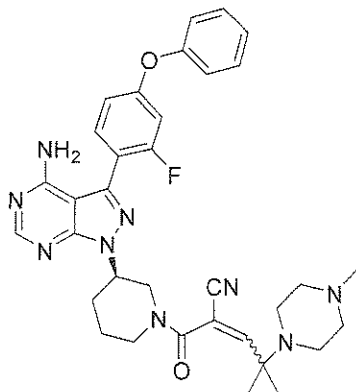
having the structure:



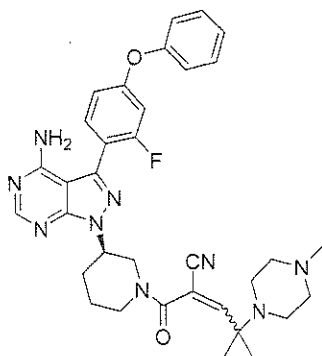
where *C is (R), (S), or a mixture of (R) and (S);

or an individual E or Z isomer of any one of the above compound.

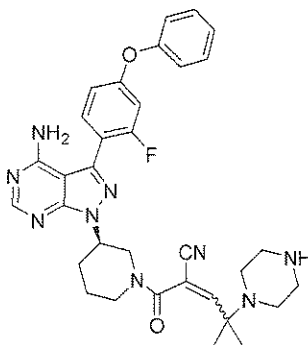
9. The compound of Claim 7 and/or a pharmaceutically acceptable salt thereof wherein the compound is (E) isomer or (Z) isomer of 2-[[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile having the structure:



10. The compound of Claim 7 and/or a pharmaceutically acceptable salt thereof wherein the compound is a mixture of (E) isomer and (Z) isomer of 2-[[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile having the structure:



11. The compound of Claim 7 and/or a pharmaceutically acceptable salt thereof wherein the compound is a mixture of (E) isomer and (Z) isomer of 2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile having the structure:



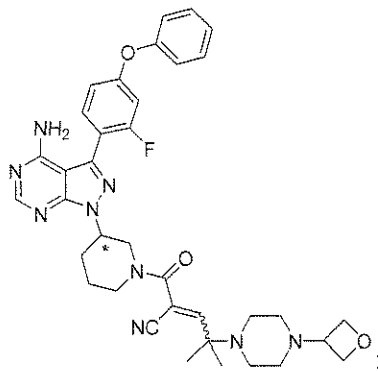
12. The compound of Claim 7 and/or a pharmaceutically acceptable salt thereof wherein the compound is:

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile; or

a mixture of (R)- 2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile and (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile;

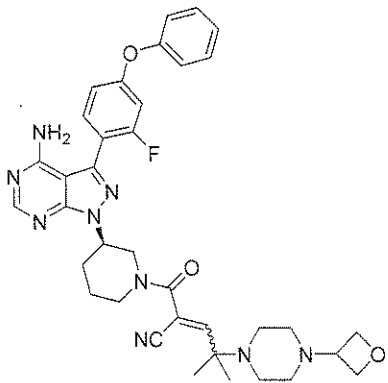
having the structure:



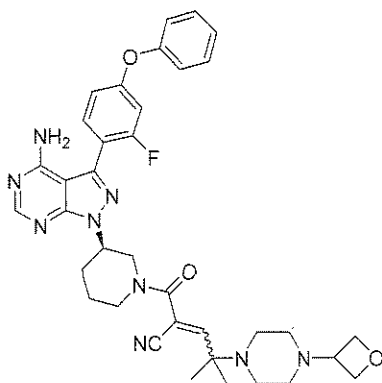
where *C is (R), (S), or a mixture of (R) and (S);

5 or an individual E or Z isomer of any one of the above compounds.

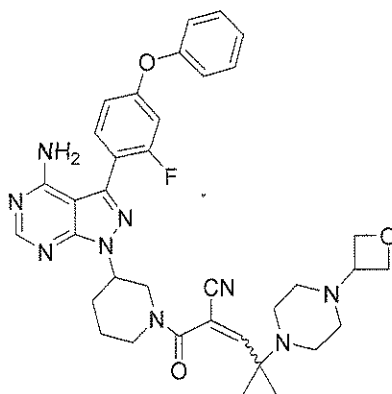
13. The compound of Claim 7 and/or a pharmaceutically acceptable salt thereof wherein the compound is (E) isomer or (Z) isomer of (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile having the structure:



14. The compound of Claim 7 and/or a pharmaceutically acceptable salt thereof wherein the compound is a mixture of (E) isomer and (Z) isomer of (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile having the structure:



15. The compound of Claim 7 and/or a pharmaceutically acceptable salt thereof wherein the compound is a mixture (S) and (R) isomers of 2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile having the structure:



16. A pharmaceutical composition comprising a compound and/or a pharmaceutically acceptable salt of any one of Claims 1 to 15 and a pharmaceutically acceptable excipient.

17. The pharmaceutical composition of Claim 16 comprising :

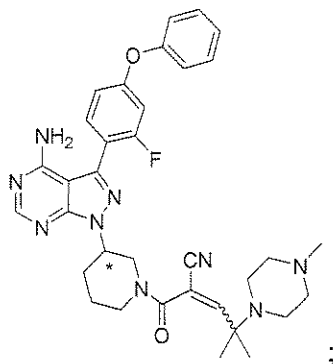
2-[[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-[[[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile; or

a mixture of 2-[[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile

and 2-[[[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

having the structure:

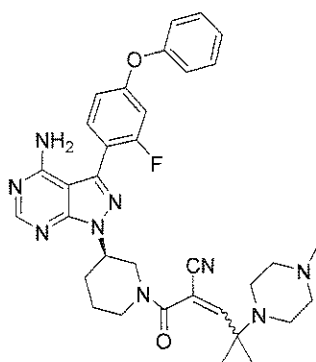


where *C is (R), (S), or a mixture of (R) and (S);

or an individual E or Z isomer of any of the above compounds; and/or

a pharmaceutically acceptable salt of any of the above compounds.

18. The pharmaceutical composition of Claim 16 comprising is a mixture of (E) isomer and (Z) isomer of 2-[[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)-pent-2-enenitrile having the structure:



and/or a pharmaceutically acceptable salt thereof.

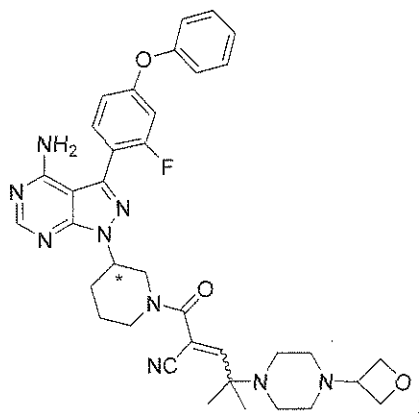
19. The pharmaceutical composition of Claim 16 comprising:

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile; or

a mixture of (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile and (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile;

having the structure:

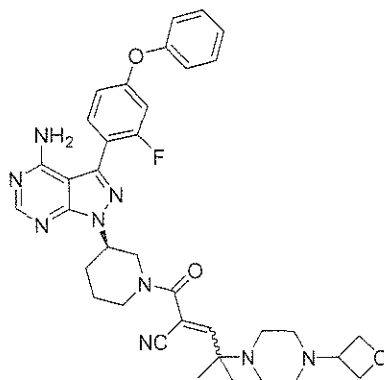


where *C is (R), (S), or a mixture of (R) and (S);

or an individual E or Z isomer of any of the above compounds; and/or

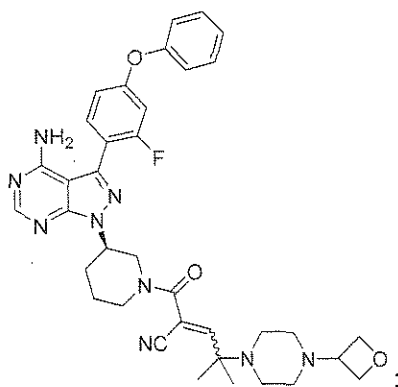
a pharmaceutically acceptable salt of any of the above compounds.

20. The pharmaceutical composition of Claim 19 comprising (E) isomer or (Z) isomer of (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile having the structure:



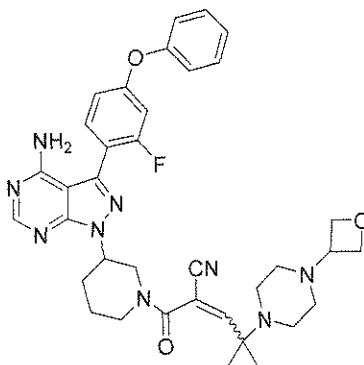
and/or a pharmaceutically acceptable salt thereof.

21. The pharmaceutical composition of Claim 19 comprising a mixture of (E) isomer and (Z) isomer of (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile having the structure:



and/or a pharmaceutically acceptable salt thereof.

22. The pharmaceutical composition of Claim 19 comprising a mixture (S) and (R) isomers of 2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile having the structure:



and/or a pharmaceutically acceptable salt thereof.

23. The pharmaceutical composition of any of the claims 16-22 wherein the pharmaceutical
5 composition is an enteric coated or delayed release formulation.
24. Use of a compound of any one of Claims 1 to 15 and/or pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of a disease treatable by inhibition of Bruton tyrosine kinase.
- 10 25. The use of Claim 24 wherein the disease is chosen from autoimmune diseases, inflammatory diseases, and cancers.
26. The use of Claim 25 wherein the disease is chosen from autoimmune diseases and
15 inflammatory diseases wherein the autoimmune disease is chosen from inflammatory bowel disease, arthritis, lupus, myasthenia gravis, Graves' disease, Sjogren's syndrome, Sjogren's dry eye, non-Sjogren's dry eye disease, multiple sclerosis, Guillain-Barre syndrome, ankylosing spondylitis, idiopathic thrombocytopenic purpura, scleroderma, warm autoimmune hemolytic anemia, Wegener's granulomatosis, and psoriasis; and the inflammatory disease is chosen from
20 asthma, colitis, conjunctivitis, Behcet's disease, atopic dermatitis, uveitis, and eczema.
27. The use of Claim 25 wherein the disease is cancer chosen from diffuse large B cell lymphoma, follicular lymphoma, chronic lymphocytic lymphoma, chronic lymphocytic leukemia, B-ALL, B-cell prolymphocytic leukemia, small lymphocytic lymphoma (SLL),
25 multiple myeloma, B-cell non-Hodgkin lymphoma, lymphoplasmacytic lymphoma/

Waldenstrom macroglobulinemia, splenic marginal zone lymphoma, plasma cell myeloma, plasmacytoma, extranodal marginal zone B cell lymphoma, nodal marginal zone B cell lymphoma, mantle cell lymphoma, mediastinal (thymic) large B cell lymphoma, intravascular large B cell lymphoma, primary effusion lymphoma, burkitt's lymphoma/leukemia, and lymphomatoid granulomatosis.

28. The use of Claim 26 wherein the disease is chosen from rheumatoid arthritis, psoriatic arthritis, lupus, uveitis, myasthenia gravis, warm autoimmune hemolytic anemia, Wegener's granulomatosis, Sjogren's disease, Sjogren's dry eye, non-Sjogren's dry eye disease, psoriasis, and asthma.

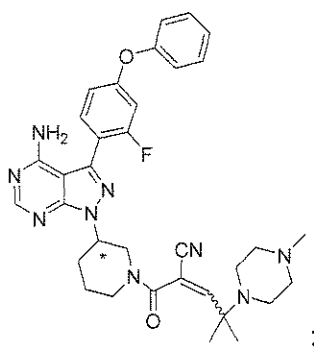
29. The use of any one of Claims 24-28 wherein the compound is:

2-[[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

2-[[[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile; or

a mixture of 2-[[[(3R)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile and 2-[[[(3S)-3-[4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]-pyrimidin-1-yl]-piperidin-1-yl]carbonyl]-4-methyl-4-(4-methylpiperazin-1-yl)pent-2-enenitrile;

having the structure:

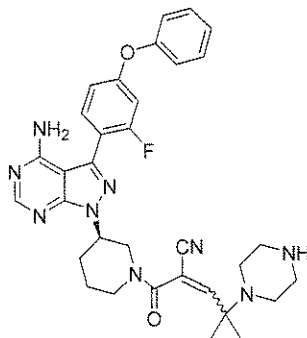


where *C is (R), (S), or a mixture of (R) and (S);

or an individual E or Z isomer of any of the above compounds; and/or

a pharmaceutically acceptable salt of any of the above compounds.

30. The use of any one of Claims 24-28 wherein the compound is a mixture of (E) isomer and (Z) isomer of 2-((R)-3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(piperazin-1-yl)pent-2-enenitrile having the structure:



and/or a pharmaceutically acceptable salt thereof.

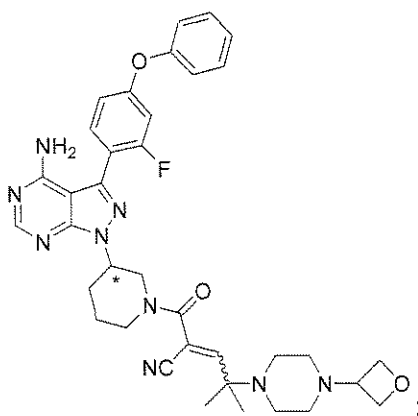
31. The use of any one of Claims 24-28 wherein the compound is:

(R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile;

(S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile; or

a mixture of (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile and (S)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enenitrile;

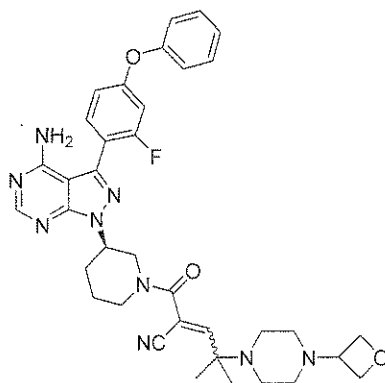
having the structure:



where *C is (R), (S), or a mixture of (R) and (S);
 or an individual E or Z isomer of any of the above compounds; and/or
 a pharmaceutically acceptable salt of any of the above compounds.

5

32. The use of any one of Claims 24-28 wherein the compound is a mixture of (E) isomer and (Z) isomer of (R)-2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enitrile having the structure:

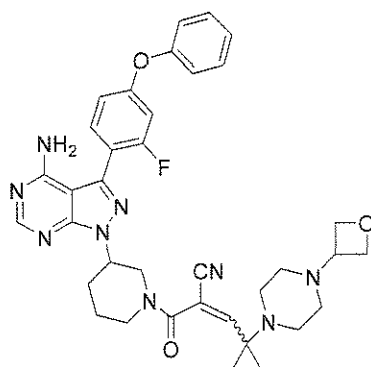


10

and/or a pharmaceutically acceptable salt thereof.

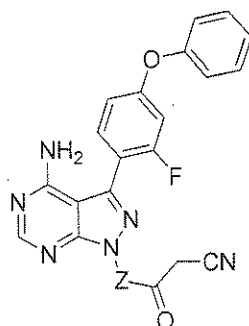
33. The use of any one of Claims 24-28 wherein the compound is wherein the compound is a mixture (S) and (R) isomers of 2-(3-(4-amino-3-(2-fluoro-4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidine-1-carbonyl)-4-methyl-4-(4-(oxetan-3-yl)piperazin-1-yl)pent-2-enitrile having the structure:

15



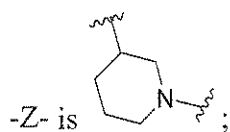
34. The use of any one of Claim 27 and 29-33 wherein the compound and/or
pharmaceutically acceptable salt is administered in combination with one or more anti-cancer or
5 anti-inflammatory agents.

35. A process of preparing a compound of any one of Claims 8, 11, and 12 comprising:
(a) reacting a compound of formula (1):



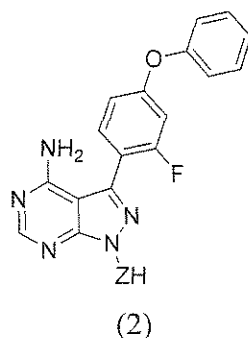
(1)

wherein:

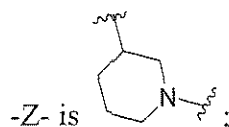


with an aldehyde of formula $R^c\text{CHO}$ where R^c is $-\text{C}(\text{CH}_3)_2\text{-(piperazin-1-yl)}$, $-\text{C}(\text{CH}_3)_2\text{-(4-methylpiperazin-1-yl)}$, or $-\text{C}(\text{CH}_3)_2\text{-4-(oxetan-3-yl)piperazin-1-yl}$; or

(b) reacting a compound of formula (2):



wherein:



with a compound of formula $R^cCH=C(CN)CO_2H$ or $R^cCH=C(CN)COX$ (where R^c is $-C(CH_3)_2$ -(piperazin-1-yl), $-C(CH_3)_2$ -(4-methylpiperazin-1-yl), or $-C(CH_3)_2$ -4-(oxetan-3-yl)piperazin-1-yl) and X is a leaving group capable of being displaced by the nitrogen atom of the Z group under amide coupling reaction conditions;

(c) optionally making an acid addition salt of a compound obtained from Steps (a) or (b) above;

(d) optionally making a free base of a compound obtained from Steps (a), (b), or (c) above;

(e) optionally separating individual stereoisomers of the compounds obtained from Steps (a), (b), (c), or (d) above; and

(f) optionally separating individual (E) and (Z) isomers of the compounds obtained from steps (a), (b), (c), (d), or (e) above.

36. The process of Claim 34 wherein R^c is $-C(CH_3)_2$ -4-(oxetan-3-yl)piperazin-1-yl.