(12) **Translation of European patent specification**

(11) **NO/EP 3129021 B1**

(19) NO

NORWAY

(51) Int Cl.
A61K 31/397 (2006.01)
A61K 31/437 (2006.01)
A61K 31/502 (2006.01)
A61K 31/519 (2006.01)
A61P 35/00 (2006.01)
A61P 35/02 (2006.01)

Norwegian Industrial Property Office

(45)	Translation Published	2020.11.23
(80)	Date of The European Patent Office Publication of the Granted Patent	2020.09.23
(86)	European Application Nr.	15717381.6
(86)	European Filing Date	2015.04.07
(87)	The European Application's Publication Date	2017.02.15
(30)	Priority	2014.04.08, US, 201461976815 P
(84)	Designated Contracting States:	AL ; AT ; BE ; BG ; CH ; CY ; CZ ; DE ; DK ; EE ; ES ; FI ; FR ; GB ; GR ; HR ; HU ; IE ; IS ; IT ; LI ; LT ; LU ; LV ; MC ; MK ; MT ; NL ; NO ; PL ; PT ; RO ; RS ; SE ; SI ; SK ; SM ; TR
	Designated Extension States:	BA ; ME
	Designated Validation States:	MA
(73)	Proprietor	Incyte Corporation, 1801 Augustine Cut-Off, Wilmington, DE 19803, USA
(72)	Inventor	SCHERLE, Peggy A., 303 Elm Avenue, Swarthmore, PA 19081, USA LIU, Xuesong, 14 Spring Valley Lane, Hockessin, Delaware 19707, USA
(74)	Agent or Attorney	OSLO PATENTKONTOR AS, Hoffsveien 1A, 0275 OSLO, Norge

(54) Title **TREATMENT OF B-CELL MALIGNANCIES BY A COMBINATION JAK AND PI3K INHIBITOR**

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Enclosed is a translation of the patent claims in Norwegian. Please note that as per the Norwegian Patents Acts, section 66i the patent will receive protection in Norway only as far as there is agreement between the translation and the language of the application/patent granted at the EPO. In matters concerning the validity of the patent, language of the application/patent granted at the EPO will be used as the basis for the decision. The patent documents published by the EPO are available through Espacenet (http://worldwide.espacenet.com) or via the search engine on our website here: https://search.patentstyret.no/

Patentkrav

1. Inhibitor av JAK1 og/eller JAK2 og inhibitor av PI3Kδ, for anvendelse i en fremgangsmåte for behandling av en sykdom valgt fra diffust stort B-celle-lymfom, aktivert B-cellelignende (ABC) diffust stort B-celle-lymfom (ABC-DLBCL), og germinal sentrum B-celle (GCB) diffust stort B-celle-lymfom (GCB-DLBCL) hos en pasient som trenger det, hvor fremgangsmåten omfatter administrasjon til nevnte pasienten: (a) en inhibitor av JAK1 og/eller JAK2; og (b) en inhibitor av PI3Kδ; hvor:

a. nevnte inhibitor av JAK1 og/eller JAK2 er valgt fra:

3-cyklopentyl-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propannitril;

3-[1-(6-kloropyridin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propannitril;

3-(1-[1,3]oksazolo[5,4-b]pyridin-2-ylpyrrolidin-3-yl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propannitril;

4-[(4-{3-cyano-2-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propyl}piperazin-1-yl)karbonyl]-3-fluorobenzonitril;

4-[(4-{3-cyano-2-[3-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrrol-1-yl]propyl}piperazin-1-yl)karbonyl]-3-fluorobenzonitril;

{1-{1-[3-Fluoro-2-(trifluorometyl)isonikotinoyl]piperidin-4-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-3-yl}acetonitril;

4-{3-(cyanometyl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-1-yl}-N-[4-fluoro-2-(trifluorometyl)fenyl]piperidin-1-karboksamid;

[3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]-1-(1-{[2-(trifluorometyl)pyrimidin-4-yl]karbonyl}piperidin-4-yl)azetidin-3-yl]acetonitril;

[*trans*-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]-3-(4-{[2-(trifluorometyl)pyrimidin-4-yl]karbonyl}piperazin-1-yl)cyklobutyl]acetonitril;

{*trans*-3-(4-{[4-[(3-hydroksyazetidin-1-yl)metyl]-6-(trifluorometyl)pyridin-2-yl]oksy}piperidin-1-yl)-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]cyklobutyl}acetonitril;

{*trans*-3-(4-{[4-{[(2S)-2-(hydroksymetyl)pyrrolidin-1-yl]metyl}-6-(trifluorometyl)pyridin-2-yl]oksy}piperidin-1-yl)-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]cyklobutyl}acetonitril;

{*trans*-3-(4-{[4-{[(2R)-2-(hydroksymetyl)pyrrolidin-1-yl]metyl}-6-(trifluorometyl)pyridin-2-yl]oksy}piperidin-1-yl)-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]cyklobutyl}acetonitril;

4-(4-{3-[(dimetylamino)metyl]-5-fluorofenoksy}piperidin-1-yl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]butannitril;

5-{3-(cyanometyl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-1-yl}-N-isopropylpyrazin-2-karboksamid;

4-{3-(cyanometyl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-1-yl}-2,5-difluoro-N-[(1S)-2,2,2-trifluoro-1-metyletyl]benzamid;

5-{3-(cyanometyl)-3-[4-(1H-pyrrolo[2,3-b]pyridin-4-yl)-1H-pyrazol-1-yl]azetidin-1-yl}-N-isopropylpyrazin-2-karboksamid;

{1-(*cis*-4-{[6-(2-hydroksyetyl)-2-(trifluorometyl)pyrimidin-4-yl]oksy}cykloheksyl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-3-yl}acetonitril;

{1-(*cis*-4-{[4-[(etylamino)metyl]-6-(trifluorometyl)pyridin-2-yl]oksy}cykloheksyl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-3-yl}acetonitril;

{1-(*cis*-4-{[4-(1-hydroksy-1-metyletyl)-6-(trifluorometyl)pyridin-2-yl]oksy}cykloheksyl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-3-yl}acetonitril;

{1-(*cis*-4-{[4-{[(3R)-3-hydroksypyrrolidin-1-yl]metyl}-6-(trifluorometyl)pyridin-2-yl]oksy}cykloheksyl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-3-yl}acetonitril;

{1-(*cis*-4-{[4-{[(3S)-3-hydroksypyrrolidin-1-yl]metyl}-6-(trifluorometyl)pyridin-2-yl]oksy}cykloheksyl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-3-yl}acetonitril;

{*trans*-3-(4-{[4-({[(1S)-2-hydroksy-1-metyletyl]amino}metyl)-6-(trifluorometyl)pyridin-2-yl]oksy}piperidin-1-yl)-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]cyklobutyl}acetonitril;

{*trans*-3-(4-{[4-({[(2R)-2-hydroksypropyl]amino}metyl)-6-(trifluorometyl)pyridin-2-yl]oksy}piperidin-1-yl)-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]cyklobutyl}acetonitril;

{*trans*-3-(4-{[4-({[(2S)-2-hydroksypropyl]amino}metyl)-6-(trifluorometyl)pyridin-2-yl]oksy}piperidin-1-yl)-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]cyklobutyl}acetonitril;

{*trans*-3-(4-{[4-(2-hydroksyetyl)-6-(trifluorometyl)pyridin-2-yl]oksy}piperidin-1-yl)-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]cyklobutyl}acetonitril;

((2R,5S)-5-{2-[(1R)-1-hydroksyetyl]-1H-imidazo[4,5-d]tieno[3,2-b]pyridin-1-yl}tetrahydro-2H-pyran-2-yl)acetonitril;

4-[3-(cyanometyl)-3-(3',5'-dimetyl-1H,1'H-4,4'-bipyrazol-1-yl)azetidin-1-yl]-2,5-difluoro-N-[(1S)-2,2,2-trifluoro-1-metyletyl]benzamid;

og farmasøytisk akseptable salter av hvilket som helst av de ovennevnte; og

b. nevnte inhibitor av PI3Kδ er valgt fra:

7-(1-(9H-purin-6-ylamino)etyl)-6-(3-fluorofenyl)-3-metyl-5H-tiazolo[3,2-a]pyrimidin-5-on;

(S)-7-(1-(9H-purin-6-ylamino)etyl)-6-(3-fluorofenyl)-3-metyl-5Htiazolo[3,2-a]pyrimidin-5-on;

4-[1-(4-amino-3-metyl-1H-pyrazolo[3,4-d]pyrimidin-1-yl)etyl]-6-kloro-2-{1-[(2S)-2-hydroksypropyl]azetidin-3-yl}-3-metoksybenzonitril;

4-[1-(4-amino-3-metyl-1H-pyrazolo[3,4-d]pyrimidin-1-yl)etyl]-6-kloro-2-[1-(2-hydroksyetyl)azetidin-3-yl]-3-metoksybenzonitril;

5-{3-[1-(4-amino-3-metyl-1H-pyrazolo[3,4-d]pyrimidin-1-yl)etyl]-6-cyano-2-etoksy-5-metylfenyl}-N,N-dimetylpyridin-2-karboksamid;

4-{3-[1-(4-amino-3-metyl-1H-pyrazolo[3,4-d]pyrimidin-1-yl)etyl]-5-kloro-2-etoksy-6-fluorofenyl}pyrrolidin-2-on;

N-{1-[5-kloro-8-(3-fluorofenyl)cinnolin-7-yl]etyl}-9H-purin-6-amin; og

4-kloro-3'-fluoro-3-metyl-6-[1-(9H-purin-6-ylamino)etyl]bifenyl-2-karbonitril;

og farmasøytisk akseptable salter av hvilket som helst av de ovennevnte.

2. Inhibitor for JAK1 og/eller JAK2 og en inhibitor av PI3Kδ for anvendelse ifølge krav 1, hvor nevnte inhibitor av JAK1 er {1-{1-[3-fluor-2-(trifluormetyl)isonikotinoyl]piperidin-4-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-3-yl}acetonitril eller farmasøytisk akseptabelt salt derav; og nevnte inhibitor av PI3Kδ er 7-(1-(9H-purin-6-ylamino)etyl)-6-(3-fluorfenyl)-3-metyl-5H-tiazolo[3,2-a]pyrimidin-5-on, eller et farmasøytisk akseptabelt salt derav.

3. Inhibitor av JAK1 og/eller JAK2 og en inhibitor av PI3Kδ for anvendelse ifølge krav 1 eller krav 2, hvor nevnte inhibitor av JAK1 er {1-{1-[3-fluor-2-(trifluormetyl)isonikotinoyl]piperidin-4-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-3-yl}acetonitril-adipinsyresalt.

4. Inhibitor av JAK1 og/eller JAK2 og en inhibitor av PI3Kδ for anvendelse ifølge krav 1, hvor nevnte inhibitor av JAK1 er 4-{3-(cyanometyl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-1-yl}-2,5-difluor-N-[(1S)-2,2,2-trifluor-1-metyletyl]benzamid, eller et farmasøytisk akseptabelt salt derav.

5. Inhibitor av JAK1 og/eller JAK2 og en inhibitor av PI3Kδ for anvendelse ifølge krav 1, hvor nevnte inhibitor av JAK1 er valgt fra:
(S)-4-(3-((S)-1-(4-amino-3-metyl-1H-pyrazolo[3,4-d]pyrimidin-1-yl)etyl)-5-klor-2-etoksy-6-fluorfenyl)pyrrolidin-2-on;
(R)-4-(3-((S)-1-(4-amino-3-metyl-1H-pyrazolo[3,4-d]pyrimidin-1-yl)etyl)-5-klor-2-etoksy-6-fluorfenyl)pyrrolidin-2-on;
(S)-4-(3-((R)-1-(4-amino-3-metyl-1H-pyrazolo[3,4-d]pyrimidin-1-yl)etyl)-5-klor-2-etoksy-6-fluorfenyl)pyrrolidin-2-on;
(R)-4-(3-((R)-1-(4-amino-3-metyl-1H-pyrazolo[3,4-d]pyrimidin-1-yl)etyl)-5-klor-2-etoksy-6-fluorfenyl)pyrrolidin-2-on;
(N-{(1S)-1-[5-klor-8-(3-fluorfenyl)cinnolin-7-yl]etyl}-9H-purin-6-amin;
og farmasøytisk akseptable salter av hvilket som helst av de ovennevnte.

6. Inhibitor av JAK1 og/eller JAK2 og inhibitor av PI3Kδ for anvendelse ifølge krav 1 eller krav 2, hvor inhibitoren av PI3Kδ er (S)-7-(1-(9H-purin-6-ylamino)etyl)-6-(3-fluorfenyl)-3-metyl-5H-tiazolo[3,2-a]pyrimidin-5-on, eller et farmasøytisk akseptabelt salt derav.

7. Inhibitor av JAK1 og/eller JAK2 og inhibitor av PI3Kδ for anvendelse ifølge krav 1 eller krav 2, hvor sykdommen er diffust stort B-celle-lymfom.

8. Inhibitor av JAK1 og/eller JAK2 og inhibitor av PI3Kδ for anvendelse ifølge krav 1 eller krav 2, hvor sykdommen er aktivert B-cellelignende (ABC) diffust stort B-celle-lymfom (ABC-DLBCL) eller germinal sentrum B-celle (GCB) diffust stort B-celle-lymfom (GCB-DLBCL).

9. Inhibitor av JAK1 og/eller JAK2 og inhibitor av PI3Kδ for anvendelse ifølge krav 1 eller krav 2, hvor nevnte inhibitor av JAK1 og/eller JAK2 og nevnte inhibitor av PI3Kδ administreres samtidig.

10. Inhibitor av JAK1 og/eller JAK2 og inhibitor av PI3Kδ for anvendelse ifølge krav 1 eller krav 2, hvor nevnte inhibitor av JAK1 og/eller JAK2 og nevnte inhibitor av PI3Kδ administreres sekvensielt.

11. Inhibitor til JAK1 og/eller JAK2 og inhibitor av PI3Kδ for anvendelse i en fremgangsmåte for behandling av diffust stort B-celle-lymfom ifølge krav 1, hvor fremgangsmåten omfatter administrasjon til pasienten av {1-{1-[3-fluor-2-(trifluormetyl)isonikotinoyl]piperidin-4-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-

1H-pyrazol-1-yl]azetidin-3-yl}acetonitril eller farmasøytisk akseptabelt salt derav; og (S)-7-(1-(9H-purin-6-ylamino)etyl)-6-(3-fluorfenyl)-3-metyl-5H-tiazolo[3,2-a]pyrimidin-5-on, eller et farmasøytisk akseptabelt salt derav.

12. Inhibitor av JAK1 og/eller JAK2 og inhibitor av PI3Kδ for anvendelse i en fremgangsmåte for behandling av diffust stort B-celle-lymfom ifølge krav 1, omfattende administrasjon til pasienten av 4-{3-(cyanometyl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-1-yl}-2,5-difluor-N-[(1S)-2,2,2-trifluor-1-metyletyl]benzamid, eller farmasøytisk akseptabelt salt derav; og 7-(1-(9H-purin-6-ylamino)etyl)-6-(3-fluorfenyl)-3-metyl-5H-tiazolo[3,2-a]pyrimidin-5-on, eller et farmasøytisk akseptabelt salt derav.

13. Inhibitor av JAK1 og/eller JAK2 og inhibitor av PI3Kδ for anvendelse ifølge krav 1, hvor nevnte inhibitor av JAK1 er ((2R,5S)-5-{2-[(1R)-1-hydroksyetyl]-1H-imidazo[4,5-d]tieno[3,2-b]pyridin-1-yl}tetrahydro-2H-pyran-2-yl)acetonitril, eller et farmasøytisk akseptabelt salt derav.

14. Inhibitor av JAK1 og/eller JAK2 og inhibitor av PI3Kδ for anvendelse ifølge krav 1, hvor nevnte inhibitor av JAK1 er 4-[3-(cyanometyl)-3-(3',5'-dimetyl-1H,1'H-4,4'-bipyrazol-1-yl)azetidin-1-yl]-2,5-difluor-N-[(1S)-2,2,2-trifluor-1-metyletyl]benzamid, eller et farmasøytisk akseptabelt salt derav.

15. Inhibitor av JAK1 og/eller JAK2 og inhibitor av PI3Kδ for anvendelse ifølge krav 1, hvor nevnte inhibitor av PI3Kδ er (R)-4-(3-((S)-1-(4-amino-3-metyl-1H-pyrazolo[3,4-d]pyrimidin-1-yl)etyl)-5-klor-2-etoksy-6-fluorfenyl)pyrrolidin-2-on, eller et farmasøytisk akseptabelt salt derav.

16. Inhibitor av JAK1 og/eller JAK2 og inhibitor av PI3Kδ for anvendelse ifølge krav 1, hvor nevnte inhibitor av PI3Kδ er (R)-4-(3-((S)-1-(4-amino-3-metyl-1H-pyrazolo[3,4-d]pyrimidin-1-yl)etyl)-5-klor-2-etoksy-6-fluorfenyl)pyrrolidin-2-on, eller et farmasøytisk akseptabelt salt derav.

17. Inhibitor av JAK1 og/eller JAK2 og inhibitor av PI3Kδ for anvendelse ifølge krav 1, hvor nevnte inhibitor av PI3Kδ er (S)-4-(3-((R)-1-(4-amino-3-metyl-1H-pyrazolo[3,4-d]pyrimidin-1-yl)etyl)-5-klor-2-etoksy-6-fluorfenyl)pyrrolidin-2-on, eller et farmasøytisk akseptabelt salt derav.

18. Inhibitor av JAK1 og/eller JAK2 og inhibitor av PI3Kδ for anvendelse ifølge krav 1, hvor nevnte inhibitor av PI3Kδ er (R)-4-(3-((R)-1-(4-amino-3-metyl-1H-pyrazolo[3,4-d]pyrimidin-1-yl)etyl)-5-klor-2-etoksy-6-fluorfenyl)pyrrolidin-2-on, eller et farmasøytisk akseptabelt salt derav.

19. Inhibitor av JAK1 og/eller JAK2 og inhibitor av PI3Kδ for anvendelse ifølge krav 1, hvor nevnte inhibitor av PI3Kδ er (S)-7-(1-(9H-purin-6-ylamino)etyl)-6-(3-fluorfenyl)-3-metyl-5H-tiazolo[3,2-a]pyrimidin-5-on, eller et farmasøytisk akseptabelt salt derav.

20. Inhibitor av JAK1 og/eller JAK2 og inhibitor av PI3Kδ, for anvendelse i kombinasjon med en inhibitor av PI3Kδ i en fremgangsmåte for behandling av en sykdom valgt fra diffust stort B-celle-lymfom, aktivert B-cellelignende (ABC) diffust stort B-celle-lymfom (ABC-DLBCL), og germinal sentrum B-celle (GCB) diffust stort B-celle-lymfom (GCB-DLBCL) hos en pasient som trenger det, hvor fremgangsmåten omfatter administrasjon til nevnte pasienten: (a) en inhibitor av JAK1 og/eller JAK2; og (b) en inhibitor av PI3Kδ; hvor:

a. nevnte inhibitor av JAK1 og/eller JAK2 er valgt fra:

3-cyklopentyl-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propannitril;

3-[1-(6-kloropyridin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propannitril;

3-(1-[1,3]oksazolo[5,4-b]pyridin-2-ylpyrrolidin-3-yl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propannitril;

4-[(4-{3-cyano-2-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propyl}piperazin-1-yl)karbonyl]-3-fluorobenzonitril;

4-[(4-{3-cyano-2-[3-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrrol-1-yl]propyl}piperazin-1-yl)karbonyl]-3-fluorobenzonitril;

{1-{1-[3-Fluoro-2-(trifluorometyl)isonikotinoyl]piperidin-4-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-3-yl}acetonitril;

4-{3-(cyanometyl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-1-yl}-N-[4-fluoro-2-(trifluorometyl)fenyl]piperidin-1-karboksamid;

[3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]-1-(1-{[2-(trifluorometyl)pyrimidin-4-yl]karbonyl}piperidin-4-yl)azetidin-3-yl]acetonitril;

[*trans*-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]-3-(4-{[2-(trifluorometyl)pyrimidin-4-yl]karbonyl}piperazin-1-yl)cyklobutyl]acetonitril;

{*trans*-3-(4-{[4-[(3-hydroksyazetidin-1-yl)metyl]-6-(trifluorometyl)pyridin-2-yl]oksy}piperidin-1-yl)-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]cyklobutyl}acetonitril;

{*trans*-3-(4-{[4-{[(2S)-2-(hydroksymetyl)pyrrolidin-1-yl]metyl}-6-(trifluorometyl)pyridin-2-yl]oksy}piperidin-1-yl)-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]cyklobutyl}acetonitril;

{*trans*-3-(4-{[4-{[(2R)-2-(hydroksymetyl)pyrrolidin-1-yl]metyl}-6-(trifluorometyl)pyridin-2-yl]oksy}piperidin-1-yl)-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]cyklobutyl}acetonitril;

4-(4-{3-[(dimetylamino)metyl]-5-fluorofenoksy}piperidin-1-yl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]butannitril;

5-{3-(cyanometyl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-1-yl}-N-isopropylpyrazin-2-karboksamid;

4-{3-(cyanometyl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-1-yl}-2,5-difluoro-N-[(1S)-2,2,2-trifluoro-1-metyletyl]benzamid;

5-{3-(cyanometyl)-3-[4-(1H-pyrrolo[2,3-b]pyridin-4-yl)-1H-pyrazol-1-yl]azetidin-1-yl}-N-isopropylpyrazin-2-karboksamid;

{1-(*cis*-4-{[6-(2-hydroksyetyl)-2-(trifluorometyl)pyrimidin-4-yl]oksy}cykloheksyl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-3-yl}acetonitril;

{1-(*cis*-4-{[4-[(etylamino)metyl]-6-(trifluormetyl)pyridin-2-yl]oksy}cykloheksyl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-3-yl}acetonitril;

{1-(*cis*-4-{[4-(1-hydroksy-1-metyletyl)-6-(trifluormetyl)pyridin-2-yl]oksy}cykloheksyl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-3-yl}acetonitril;

{1-(*cis*-4-{[4-{[(3R)-3-hydroksypyrrolidin-1-yl]metyl}-6-(trifluormetyl)pyridin-2-yl]oksy}cykloheksyl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-3-yl}acetonitril;

{1-(*cis*-4-{[4-{[(3S)-3-hydroksypyrrolidin-1-yl]metyl}-6-(trifluormetyl)pyridin-2-yl]oksy}cykloheksyl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]azetidin-3-yl}acetonitril;

{*trans*-3-(4-{[4-({[(1S)-2-hydroksy-1-metyletyl]amino}metyl)-6-(trifluormetyl)pyridin-2-yl]oksy}piperidin-1-yl)-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]cyklobutyl}acetonitril;

{*trans*-3-(4-{[4-({[(2R)-2-hydroksypropyl]amino}metyl)-6-(trifluormetyl)pyridin-2-yl]oksy}piperidin-1-yl)-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]cyklobutyl}acetonitril;

{*trans*-3-(4-{[4-({[(2S)-2-hydroksypropyl]amino}metyl)-6-(trifluormetyl)pyridin-2-yl]oksy}piperidin-1-yl)-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]cyklobutyl}acetonitril;

{*trans*-3-(4-{[4-(2-hydroksyetyl)-6-(trifluormetyl)pyridin-2-yl]oksy}piperidin-1-yl)-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]cyklobutyl}acetonitril;

((2R,5S)-5-{2-[(1R)-1-hydroksyetyl]-1H-imidazo[4,5-d]tieno[3,2-b]pyridin-1-yl}tetrahydro-2H-pyran-2-yl)acetonitril;

4-[3-(cyanometyl)-3-(3',5'-dimetyl-1H,1'H-4,4'-bipyrazol-1-yl)azetidin-1-yl]-2,5-difluoro-N-[(1S)-2,2,2-trifluoro-1-metyletyl]benzamid;

og farmasøytisk akseptable salter av hvilket som helst av de ovennevnte; og

b. nevnte inhibitor av PI3Kδ er valgt fra:

7-(1-(9H-purin-6-ylamino)etyl)-6-(3-fluorofenyl)-3-metyl-5H-tiazolo[3,2-a]pyrimidin-5-on;

(S)-7-(1-(9H-purin-6-ylamino)etyl)-6-(3-fluorofenyl)-3-metyl-5Htiazolo[3,2-a]pyrimidin-5-on;

4-[1-(4-amino-3-metyl-1H-pyrazolo[3,4-d]pyrimidin-1-yl)etyl]-6-kloro-2-{1-[(2S)-2-hydroksypropyl]azetidin-3-yl}-3-metoksybenzonitril;

4-[1-(4-amino-3-metyl-1H-pyrazolo[3,4-d]pyrimidin-1-yl)etyl]-6-kloro-2-[1-(2-hydroksyetyl)azetidin-3-yl]-3-metoksybenzonitril;

5-{3-[1-(4-amino-3-metyl-1H-pyrazolo[3,4-d]pyrimidin-1-yl)etyl]-6-cyano-2-etoksy-5-metylfenyl}-N,N-dimetylpyridin-2-karboksamid;

4-{3-[1-(4-amino-3-metyl-1H-pyrazolo[3,4-d]pyrimidin-1-yl)etyl]-5-kloro-2-etoksy-6-fluorofenyl}pyrrolidin-2-on;

N-{1-[5-kloro-8-(3-fluorofenyl)cinnolin-7-yl]etyl}-9H-purin-6-amin; og

4-kloro-3'-fluoro-3-metyl-6-[1-(9H-purin-6-ylamino)etyl]bifenyl-2-karbonitril;

og farmasøytisk akseptable salter av hvilket som helst av de ovennevnte.