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Norwegian Industrial Property Office

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(62)	Divided application	EP3277681, 2016.03.31
(73)	Proprietor	Merck Patent GmbH, Frankfurter Strasse 250, 64293 Darmstadt, Tyskland
(72)	Inventor	Fuchss, Thomas, Jahnstrasse 12, 64625 BENSHEIM-AUERBACH, Tyskland Schiemann, Kai, Am Roedergraben 8, 64342 SEEHEIM-JUGENHEIM, Tyskland
(74)	Agent or Attorney	TANDBERG INNOVATION AS, Postboks 1570 Vika, 0118 OSLO, Norge

(54) Title **IMIDAZOLONYL QUINOLINES AND THEIR USE AS ATM KINASE INHIBITORS**

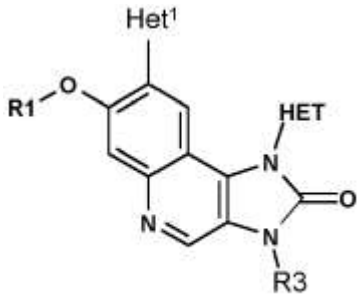
(56) References Cited:

WO-A1-2011/054846
WO-A1-2010/139731

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. Forbindelse med formelen (I)



(I)

hvor

R1 er metyl,

R3 betyr uforgrenet eller forgrenet alkyl med 1, 2, eller 3 C-atomer, hvor 1, 2, 3, 4, eller 5 H-atomer uavhengig av hverandre kan være erstattet av Hal,

Het^1 er valgt fra pyrazolyl, triazolyl og imidazolyl, hvor Het^1 er usubstituert eller substituert med én eller to substituenter som uavhengig av hverandre er valgt fra alkyl som kan være usubstituert eller substituert én eller flere ganger med halogen, -OY, -NYY, Hal og $-Het^2$,

HET betyr en 5-leddet énkjernet aromatisk heterosyklus, hvor denne heterosyklusen er knyttet sammen med N-atomet til skjelettet via et ring-C-atom, hvor denne heterosyklusen er valgt fra pyrazolyl, tiazolyl og imidazolyl, og kan være usubstituert eller substituert ved én, to eller tre substituenter som uavhengig av hverandre er valgt fra gruppen bestående av: Hal, A, Het^2, $-(CY_2)_p-OY$, $-(CY_2)_p-OZ$, $-(CY_2)_p-O-Het^2$ $-(CY_2)_p-O-(CY_2)_t-Het^2$, $-(CY_2)_p-O-(CY_2)_t-NYY$, $-(CY_2)_p-O-(CY_2)_t-OY$, $-(CY_2)_p-NYY$, $-(CY_2)_p-COOY$, $-(CY_2)_p-CO-NYY$, og $-(CY_2)_p-NY-COY$,

A henholdsvis uavhengig betyr uforgrenet eller forgrenet alkyl med 1, 2, 3, 4, 5, 6, 7, 8, 9 eller 10 C-atomer, hvor 1, 2, 3, 4, 5, 6 eller 7 H-atomer uavhengig av hverandre kan være erstattet av Hal,

Het^2 betyr en énkjernet mettet heterosyklus med 2, 3, 4, 5, 6 eller 7 C-atomer og 1, 2, 3 eller 4 N-, O- og/eller S-atomer som kan være usubstituert eller enkelt substituert med A,

Y betyr H eller A,

Z betyr uforgrenet eller forgrenet alkenyl med 2, 3, 4, 5, 6, 7, 8, 9 eller 10 C-atomer, hvor 1, 2, 3, 4, 5, 6 eller 7 H-atomer uavhengig av hverandre kan være erstattet av Hal,
Hal betyr F, Cl, Br eller I, og
p, 0, 1, 2, 3, 4, 5 eller 6
t betyr 1, 2, 3, 4, 5 eller 6,
og/eller farmasøytisk anvendbart salt, solvat, tautomerer, stereoisomerer derav.

2. Forbindelse med formelen (I) ifølge krav 1, hvor HET kan være substituert med én, to eller tre substituenter som uavhengig av hverandre er valgt fra gruppen bestående av: F, Cl, metyl, etyl, propyl, isopropyl, metoksy, etoksy, propoksy, piperazinyl, tetrahydropyranyl, 2-metoksyetoksy, 2-hydroksyetoksy, fluormetoksy, difluormetoksy, N-metylkarbamoyl (-C(=O)-NH-CH_3), 2-metylamino-etoksy, 1-metyl-azetidin-3-ylmetoksy, trideuteriometoksy, trifluormetoksy, allyloksy og azetidinyloksy og/eller farmasøytisk anvendbart salt, solvat, tautomerer, stereoisomerer derav.

3. Forbindelse med formelen (I) ifølge krav 1 eller 2, hvor HET er valgt fra: 1H-pyrazol-4-yl, 1-etyl-3-metyl-1H-pyrazol-4-yl, 1,2-dimetyl-1H-pyrazol-4-yl, 1,3-dimetyl-1H-pyrazol-4-yl, 1-metyl-1H-pyrazol-4-yl, 1-(tetrahydropyran-4-yl)-1H-pyrazol-4-yl, 2-metyl-2H-pyrazol-3-yl, 3-metyl-1H-pyrazol-4-yl, 2-metyl-tiazol-4-yl, 3,5-dimetyl-1H-pyrazol-4-yl, 3-fluor-1-metyl-pyrazol-4-yl, tiazol-2-yl og 1-metyl-1H-imidazolyl og/eller farmasøytisk anvendbart salt, solvat, tautomerer, stereoisomerer derav.

4. Forbindelse med formelen (I) ifølge krav 1, 2 eller 3, hvor Het^1 er pyrazolyl som kan være usubstituert eller substituert som definert i krav 1, og/eller farmasøytisk anvendbart salt, solvat, tautomerer, stereoisomerer derav.

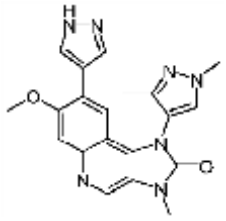
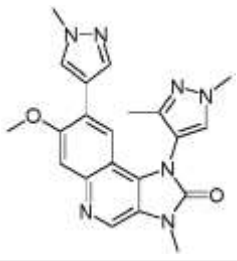
5. Forbindelse med formelen (I) ifølge krav 1, 2 eller 3, hvor Het^1 er triazolyl, foretrukket [1,2,3]triazolyl som kan være usubstituert eller substituert som definert i krav 1 eller 2, og/eller farmasøytisk anvendbart salt, solvat, tautomerer, stereoisomerer derav.

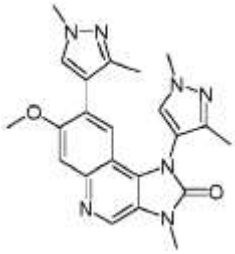
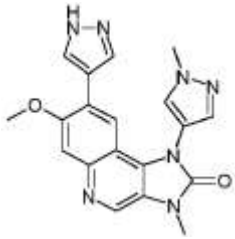
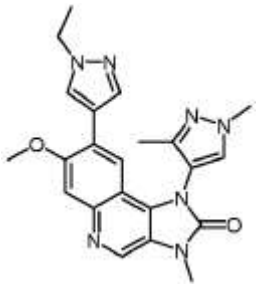
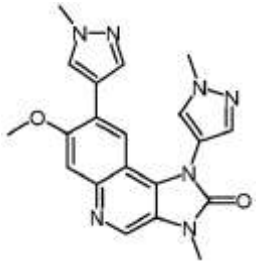
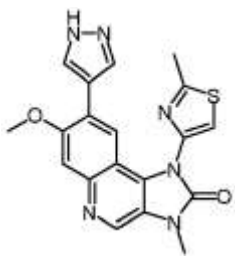
6. Forbindelse med formelen (I) ifølge et av kravene 1 til 4, hvor Het^1 er usubstituert eller substituert med én eller to substituenter som uavhengig av hverandre er valgt fra metyl, etyl, amino, metoksy, fluormetyl, difluormetyl, fluor, azetidinyl, og/eller farmasøytisk anvendbart salt, solvat, tautomerer, stereoisomerer derav.

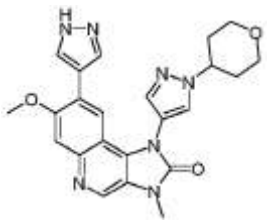
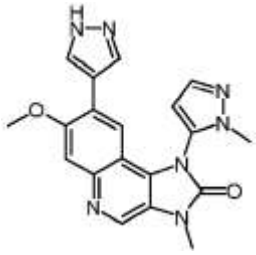
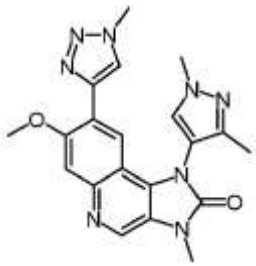
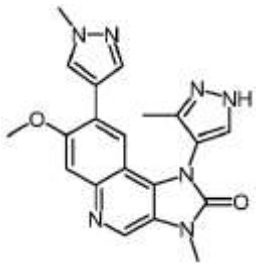
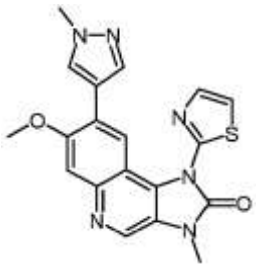
7. Forbindelse med formelen (I) ifølge et av kravene 1 til 4, hvor Het^1 er valgt fra: 1H-pyrazol-4-yl, 2H-pyrazol-3-yl, 1H-pyrazol-3-yl, 1-metyl-1H-pyrazol-4-yl, 3-metyl-1H-pyrazol-4-yl, 5-metyl-1H-pyrazol-3-yl, 4-metyl-1H-pyrazol-3-yl, 1-fluormetyl-1H-pyrazol-4-yl, 1-difluormetyl-1H-pyrazol-4-yl, 1,3-dimetyl-1H-pyrazol-4-yl, 1-etyl-1H-pyrazol-4-yl, 1-etyl-3-metyl-1H-pyrazolyl, 3-fluor-1-metyl-1H-pyrazol-4-yl, 3-amino-1H-pyrazol-5-yl, 2H-[1,2,3]triazol-4-yl, 3H-[1,2,3]triazol-4-yl-, 1-metyl-1H-[1,2,3]triazol-4-yl, 2-metyl-2H-[1,2,3]triazol-4-yl, 2-amino-1H-imidazol-4-yl og 1-(azetidin-3-yl)-3-metyl-1H-pyrazol-4-yl og/eller farmasøytisk anvendbart salt, solvat, tautomerer, stereoisomerer derav.

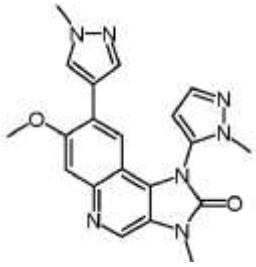
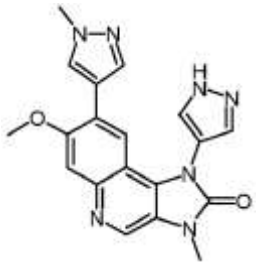
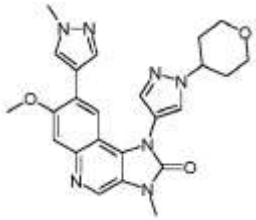
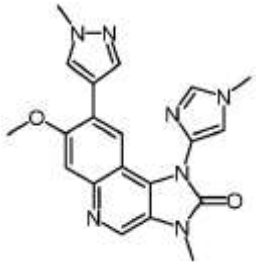
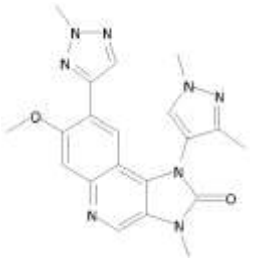
8. Forbindelse med formelen (I) ifølge et av kravene 1 til 7, hvor R3 betyr metyl og/eller farmasøytisk anvendbart salt, solvat, tautomerer, stereoisomerer derav.

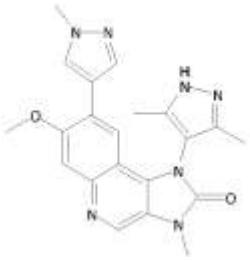
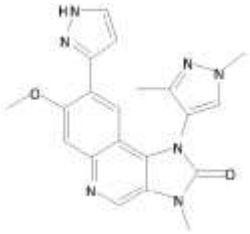
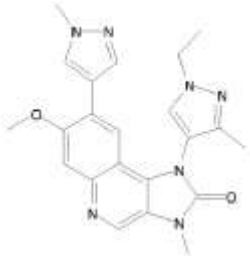
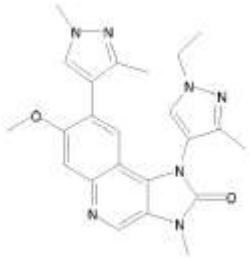
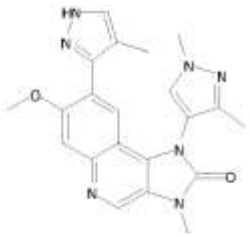
9. Forbindelse ifølge krav 1, valgt fra:

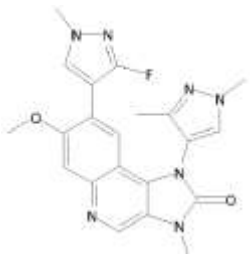
	1-(1,3-dimetyl-1 H-pyrazol-4-yl)-7-metoksy-3-metyl-8-(1 H-pyrazol-4-yl)-1,3-dihydro-imidazo[4,5-c]kinolin-2-on
	1-(1,3-dimetyl-1 H-pyrazol-4-yl)-7-metoksy-3-metyl-8-(1-metyl-1 H-pyrazol-4-yl)-1,3-dihydro-imidazo[4,5-c]kinolin-2-on

	1,8-bis-(1,3-dimetyl-1 H-pyrazol-4-yl)-7-metoksy-3-metyl-1,3-dihydro-imidazo[4,5-c]kinolin-2-on
	7-metoksy-3-metyl-1-(1-metyl-1 H-pyrazol-4-yl)-8-(1 H-pyrazol-4-yl)-1,3-dihydro-imidazo[4,5-c]kinolin-2-on
	1-(1,3-dimetyl-1 H-pyrazol-4-yl)-8-(1-etyl-1 H-pyrazol-4-yl)-7-metoksy-3-metyl-1,3-dihydro-imidazo[4,5-c]kinolin-2-on
	7 -metoksy-3-metyl-1, 8-bis-(1-metyl-1 H-pyrazol-4-yl)-1,3-dihydro-imidazo[4,5-c]kinolin-2-on
	7-metoksy-3-metyl-1-(2-metyl-tiazol-4-yl)-8-(1 H-pyrazol-4-yl)-1, 3-dihydro-imidazo[4,5-c]kinolin-2-on

	7-metoksy-3-metyl-8-(1 H-pyrazol-4-yl)-1-[1-(tetrahydro-pyran-4-yl)-1 H-pyrazol-4-yl]-1,3-dihydro-imidazo[4,5-c]kinolin-2-on
	7-metoksy-3-metyl-1-(2-metyl-2H-pyrazol-3-yl)-8-(1 H-pyrazol-4-yl)-1,3-dihydro-imidazo[4,5-c]kinolin-2-on
	1-(1,3-dimetyl-1 H-pyrazol-4-yl)-7-metoksy-3-metyl-8-(1-metyl-1 H-[1,2,3]triazol-4-yl)-1,3-dihydro-imidazo[4,5-c]kinolin-2-on
	7-metoksy-3-metyl-1-(3-metyl-1 H-pyrazol-4-yl)-8-(1-metyl-1 H-pyrazol-4-yl)-1,3-dihydro-imidazo[4,5-c]kinolin-2-on
	7-metoksy-3-metyl-8-(1-metyl-1 H-pyrazol-4-yl)-1-tiazol-2-yl-1,3-dihydro-imidazo[4,5-c]kinolin-2-on

	7-metoksy-3-metyl-1-(2-metyl-2H-pyrazol-3-yl)-8-(1-metyl-1H-pyrazol-4-yl)-1,3-dihydro-imidazo[4,5-c]kinolin-2-on
	7-metoksy-3-metyl-8-(1-metyl-1 H-pyrazol-4-yl)-1-(1 H-pyrazol-4-yl)-1 ,3-dihydro-imidazo[4,5-c]kinolin-2-on
	7-metoksy-3-metyl-8-(1-metyl-1 H-pyrazol-4-yl)-1-[1-(tetrahydro-pyran-4-yl)-1 H-pyrazol-4-yl]-1,3-dihydro-imidazo[4,5-c]kinolin-2-on
	7-metoksy-3-metyl-1-(1-metyl-1 H-imidazol-4-yl)-8-(1-metyl-1 H-pyrazol-4-yl)-1,3-dihydro-imidazo[4,5-c]kinolin-2-on
	1-(1,3-dimetyl-1 H-pyrazol-4-yl)-7-metoksy-3-metyl-8-(2-metyl-2H-[1,2,3]triazol-4-yl)-1,3-dihydro-imidazo[4,5-c]kinolin-2-on

	1-(3,5-dimetyl-1 H-pyrazol-4-yl)-7-metoksy-3-metyl-8-(1-metyl-1 H-pyrazol-4-yl)-1,3-dihydro-imidazo[4,5-c]kinolin-2-on
	1-(1,3-dimetyl-1 H-pyrazol-4-yl)-7-metoksy-3-metyl-8-(1 H-pyrazol-3-yl)-1,3-dihydro-imidazo[4,5-c]kinolin-2-on
	1-(1-etyl-3-metyl-1 H-pyrazol-4-yl)-7-metoksy-3-metyl-8-(1-metyl-1 H-pyrazol-4-yl)-1,3-dihydro-imidazo[4,5-c]kinolin-2-on
	8-(1,3-dimetyl-1 H-pyrazol-4-yl)-1-(1-etyl-3-metyl-1 H-pyrazol-4-yl)-7-metoksy-3-metyl-1,3-dihydro-imidazo[4,5-c]kinolin-2-on
	1-(1,3-dimetyl-1 H-pyrazol-4-yl)-7-metoksy-3-metyl-8-(4-metyl-1 H-pyrazol-3-yl)-1,3-dihydro-imidazo[4,5-c] kinolin-2-on

	1-(1,3-dimetyl-1 H-pyrazol-4-yl)-7-metoksy-3-metyl-8-(3-fluor-1-metyl-1 H-pyrazol-4-yl)-1,3-dihydro-imidazo[4,5-c]kinolin-2-on

og/eller farmasøytisk anvendbart salt, solvat, tautomerer, stereoisomerer derav.

10. Forbindelse ifølge et av kravene 1 til 9 og/eller farmasøytisk anvendbart salt, solvat, tautomerer eller stereoisomerer derav, for anvendelse som medikament.

11. Forbindelse ifølge et av kravene 1 til 9 og/eller farmasøytisk anvendbart salt, solvat, tautomerer eller stereoisomerer derav, for anvendelse ved behandlingen av kreft, tumorer og/eller metastaser, eventuelt i kombinasjon med radioterapi eller minst ett antikreftmiddel.

12. Forbindelse ifølge et av kravene 1 til 9 og/eller farmasøytisk anvendbart salt, solvat, tautomerer eller stereoisomerer derav, for anvendelse i sensibiliseringen av kreftceller overfor et antikreftmiddel og/eller ioniserende stråling.

13. Farmasøytisk sammensetning som inneholder en effektiv mengde av en forbindelse ifølge et av kravene 1 til 9 og/eller farmasøytisk anvendbart salt, solvat, tautomerer eller stereoisomerer derav, eventuelt sammen med minst ett farmasøytisk akseptabelt hjelpestoff.

14. Sett som består av separate pakninger av
(a) en effektiv mengde av en forbindelse ifølge et av kravene 1 til 9 og/eller farmasøytisk anvendbart salt, solvat, tautomerer eller stereoisomerer derav og
(b) en effektiv mengde av et antikreftmiddel.