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(54) Title: COMBINATION COMPRISING PURINE DERIVATIVES AND OTHER COMPOUNDS AND THE USE THEREOF FOR THE TREATMENT OF INFLAMMATORY AND OBSTRUCTIVE AIRWAY DISEASES

(57) Abstract: A medicament comprising, separately or together: a component (A) which is an adenosine A_{2a} receptor agonist as defined in the specification; and a component (B) which is one or more compounds selected from: (i) a corticosteroid, (ii) a beta-2 adrenoceptor agonist, (iii) an antimuscarinic agent, (iv) an A 2B antagonist, (v) an antihistamine, (vi) a caspase inhibitor, (vii) an ENaC inhibitor, (viii) an LTB₄ antagonist, (ix) an LTD₄ antagonist, (x) a serine protease inhibitor, (xi) a PDE4 inhibitor and (xii) a dual-acting beta-2 adrenoceptor agonist / muscarinic antagonist, for simultaneous, sequential or separate administration in the treatment of an inflammatory or obstructive airways disease.



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INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/52 A61P29/00 A61P11/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2006/045552 A (NOVARTIS AG [CH]; NOVARTIS PHARMA GMBH [AT]; FAIRHURST ROBIN ALEC [GB]) 4 May 2006 (2006-05-04) claims 7,9,13 page 45, compound Nr. 78 page 32, line 15 - page 34, line 3 -----	1-3,5-9
P,X	WO 2007/121917 A (NOVARTIS AG [CH]; NOVARTIS PHARMA GMBH [AT]; FAIRHURST ROBIN ALEC [GB]) 1 November 2007 (2007-11-01) claims 1,3,7 page 3, second compound page 12, line 10 - page 14, line 10 ----- -/--	1-3,5-9

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

* & * document member of the same patent family

Date of the actual completion of the international search

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 2007/121921 A (NOVARTIS AG [CH]; NOVARTIS PHARMA GMBH [AT]; FAIRHURST ROBIN ALEC [GB]) 1 November 2007 (2007-11-01) claims 1,7 page 29, line 21 - line 22 page 32, line 35 - page 34, line 28 -----	1-3,5-9
P,X	WO 2007/121924 A (NOVARTIS AG [CH]; NOVARTIS PHARMA GMBH [AT]; FAIRHURST ROBIN ALEC [GB]) 1 November 2007 (2007-11-01) claims 8,10,13 page 35, line 11 - page 37, line 5 -----	1-3,5-9
P,X	WO 2007/121920 A (NOVARTIS AG [CH]; NOVARTIS PHARMA GMBH [AT]; FAIRHURST ROBIN ALEC [GB]) 1 November 2007 (2007-11-01) claims 6,11 page 30, line 15 - page 32, line 17 -----	1-3,5-9

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2008/063869

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see annex

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-3 (partially), 4, 5 - 9 (partially)

A medicament comprising (A) compound Nr. 1
(((1S,2R,3S,4R)-4-{6-(2,2-diphenyl-ethylamino)-2-[(R)-3-(3-pyridin-3-yl-ureido)-pyrrolidin-1-yl]-purine-9-yl}-2,3-dihydroxy-cyclopentyl)-carbamic acid methyl ester) and one or more compounds (B)

2. claims: 1-3 and 5 - 9 (partially)

A medicament comprising (A) compound Nr. 2
(Cyclopropanecarboxylic acid
((1S,2R,3S,4R)-4-{6-(2,2-diphenyl-ethylamino)-2-[(R)-3-(3-pyridin-3-yl-ureido)-pyrrolidin-1-yl]-purine-9-yl}-2,3-dihydroxy-cyclopentyl)-amide) and one or more compounds (B)

3. claims: 1-3 and 5 - 9 (partially)

A medicament comprising (A) compound Nr. 3
(N-((1S,2R,3S,4R)-4-{6-(2,2-diphenyl-ethylamino)-2-[(R)-3-(3-pyridin-2-ylmethyl-ureido)-pyrrolidin-1-yl]-purine-9-yl}-2,3-dihydroxy-cyclopentyl)-propionamide trifluoroacetate) and one or more compounds (B)

4. claims: 1-3 and 5 - 9 (partially)

A medicament comprising (A) compound Nr. 4
(N-[(1S,2R,3S,4R)-4-(6-((S)-1-benzyl-2-hydroxy-ethylamino)-2-{(R)-3-[3-(4-sulfamoyl-phenyl)-ureido]-pyrrolidin-1-yl}-purine-9-yl)-2,3-dihydroxy-cyclopentyl]-2-hydroxyacetamide) and one or more compounds (B)

5. claims: 1-3 and 5 - 9 (partially)

A medicament comprising (A) compound Nr. 5
([(1S,2R,3S,4R)-4-(6-(2,2-diphenyl-ethylamino)-2-{(R)-3-[3-(3-sulfamoyl-phenyl)-ureido]-pyrrolidin-1-yl}-purine-9-yl)-2,3-dihydroxy-cyclopentyl]-carbamic acid methyl ester) and one or more compounds (B)

6. claims: 1-3 and 5 - 9 (partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A medicament comprising (A) compound Nr. 6
(N,N'-(1S,1S',2R,2R',3S,3S',4R,4R')-4,4'-((S)-2,2'-((3R,3R')
-3,3'-carbonylbis(azanediyl)bis(pyrrolidine-3,1-diyl))bis(6-
((S)-1-hydroxy-3-phenylpropan-2-ylamino)9H-purine-9,2-diyl))
bis(2,3-dihydroxycyclopentane-4,1-diyl)bis(2-hydroxyacetamid
e)) and one or more compounds (B)

7. claims: 1-3 and 5 - 9 (partially)

A medicament comprising (A) compound Nr. 7
(N,N'-(1S,1S',2R,2R',3S,3S',4R,4R')-4,4'-(6,6'-(1R,4R)-cyclo
hexane-1,4-diylbis(azanediyl)bis(2-(2-(1-methyl-1H-imidazol-
4-yl)ethylamino)-9H-purine-9,6-diyl))bis(2,3-dihydroxycyclop
entane-4,1-diyl(bis(2-hydroxyacetamide))) and one or more
compounds (B)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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