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60/229,715 31 August 2000 (31.08.2000) US
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(54) Title: NOVEL AUTOINDUCER MOLECULES AND USES THEREFOR

(57) Abstract: Novel bacterial quinolone signal molecules and, more particularly, pseudomonas quinolone signal ("PQS") molecules, e.g., 2-heptyl-3-hydroxy-4-quinolone, and analogs and derivatives thereof are described. Therapeutic compositions containing the molecules, and therapeutic methods, methods of for regulating gene expression, methods for identifying modulators of the autoinducer molecules, and methods of modulating quorum sensing signalling in bacteria using the compounds of the invention are also described.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C07D215/00 C07D311/04 C07D335/06

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)
 IPC 7 C07D

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, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	WO 95 28929 A (RPMS TECHNOLOGY LTD ;TAYLOR GRAHAM WALTER (GB); LACEY SANDRA LYNN) 2 November 1995 (1995-11-02) claims 1-11 ---	2-19,63, 64
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Further documents are listed in the continuation of box C.

Patent family members are listed in 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
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- *Z* document member of the same patent family

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6 March 2002

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International Application No

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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.
X	PATENT ABSTRACTS OF JAPAN vol. 1995, no. 10, 30 November 1995 (1995-11-30) & JP 07 188208 A (KAO CORP), 25 July 1995 (1995-07-25) compound (1) abstract ---	2-19
X	PATENT ABSTRACTS OF JAPAN vol. 1999, no. 05, 31 May 1999 (1999-05-31) & JP 11 029430 A (KAO CORP), 2 February 1999 (1999-02-02) abstract ---	2-19
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X	CORNFORTH J W ET AL: "STRUCTURE OF A NATURALLY OCCURRING ANTAGONIST OF DIHYDROSTREPTOMYCIN" THE BIOCHEMICAL JOURNAL, CAMBRIDGE UNIVERSITY PRESS, vol. 63, 1956, pages 124-130, XP001061524 formulae (I) and (II), 2n-heptyl, octyl, nonyl, and undecyl -4-hydroxyquinolone N-oxide ---	2-19
X	BUDZIKIEWICZ H ET AL: "BAKTERIENINHALTSSTOFFE, V: ALKYLCHINOLINE UND DEREN N-OXIDE AUS SEUDOMONAS AERUGINOSA BACTERIAL CONSTITUENTS, V: ALKYL QUINOLINES AND THEIR N-OXIDES FROM SEUDOMONAS AERUGINOSA" MONATSFESTE FUR CHEMIE, SPRINGER VERLAG. WIEN, AT, vol. 110, 1979, pages 947-952, XP001055299 ISSN: 0026-9247 compounds 3-6, 9, 10 ---	2-19
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INTERNATIONAL SEARCH REPORT

International Application No

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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.
X	SOMANATHAN R ET AL: "SYNTHESIS OF SOME 2-ALKYL-4-QUINOLONE AND 2-ALKYL-METHOXYQUINOLINE ALKALOIDS" JOURNAL OF HETEROCYCLIC CHEMISTRY, HETEROCORPORATION. PROVO, US, vol. 18, October 1981 (1981-10), pages 1077-1079, XP001056333 ISSN: 0022-152X compound (1)-(15) ---	2-19
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X	BONINI B F ET AL: "SYNTHESIS AND PROPERTIES OF A NEW FAMILY OF CHIRAL MESOGENS CONTAINING THE 2,3-DIHYDROBENZOPYRAN NUCLEUS" JOURNAL OF ORGANIC CHEMISTRY, AMERICAN CHEMICAL SOCIETY. EASTON, US, vol. 59, no. 20, 1994, pages 5930-5936, XP001061500 ISSN: 0022-3263 compounds 3a-c --- -/--	2-19

INTERNATIONAL SEARCH REPORT

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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.
X	GUILHON G M S P ET AL: "2-ALKYL-4-QUINOLONE ALKALOIDS AND CINNAMIC ACID DERIVATIVES FROM ESENBECKIA ALMAWILLIA" PHYTOCHEMISTRY, PERGAMON PRESS, GB, vol. 37, no. 4, 1994, pages 1193-1195, XP001026400 ISSN: 0031-9422 compounds (3a)-(3c)	2-19
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A	WO 99 65889 A (RES AND DEV I ;LIVINGHOUSE TOM (US)) 23 December 1999 (1999-12-23) the whole document & EP 1 087 957 A 4 April 2001 (2001-04-04)	2-19, 63, 64
A	US 5 591 872 A (PEARSON JAMES P ET AL) 7 January 1997 (1997-01-07) the whole document	2-19, 63, 64

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1, 14-16, 20-62

Present claim 1 relates to an extremely large number of possible compounds due to the moiety Q which is "tail group" and as such defined that a lack of clarity and conciseness within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claim impossible. The same holds for the compounds of claims 29-34 which are i.a. dependent on claim 1. Consequently, the search has been restricted to the compounds of claim 2. Likewise, claims 35-45, 55 and 56 which are referring to the compounds of claim 1 were not searched, too.

The initial phase of the search for the compounds of claims 14-16 (wherein Q is specified but with a very broad meaning) revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of said product claims may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of said claims is impossible.

Claims 20-28 are also not complying with Article 6 PCT since the formulation "...molecule comprising a compound..." ist not clear and therefore were not searched. Consequently claims 46-54 which are referring to the compounds of claim 20 could not be searched, too.

The "inhibitors" claimed in claim 57 and the "analogs" claimed in claims 58-62 relate to products defined by reference to a desirable characteristic or property, namely the autoinducer activity of 2-heptyl-3-hydroxy-4-quinolone or the inhibition of the induction of virulence factors by 2-heptyl-3-hydroxy-4-quinolone. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds to be claimed by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search impossible.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/27165

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