

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
21 February 2002 (21.02.2002)

PCT

(10) International Publication Number  
**WO 02/014511 A3**

(51) International Patent Classification<sup>7</sup>: **C12N 15/12**,  
15/63, 1/19, 15/11, 15/62, C07K 14/705, 16/28, C12Q  
1/68, G01N 33/68, A61K 31/7088, 38/17, 39/395, 48/00

(21) International Application Number: PCT/EP01/09243

(22) International Filing Date: 10 August 2001 (10.08.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/224,989 14 August 2000 (14.08.2000) US

(71) Applicant (for all designated States except US): **BAYER AKTIENGESELLSCHAFT** [DE/DE]; 51368 Leverkusen (DE).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **RAMAKRISHNAN, Shyam** [IN/US]; 76 Euston Road, Apt. #10, Brighton, MA 02135 (US).

(74) Common Representative: **BAYER AKTIENGESELLSCHAFT**; 51368 Leverkusen (DE).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,

CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- entirely in electronic form (except for this front page) and available upon request from the International Bureau

(88) Date of publication of the international search report:  
11 July 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: REGULATION OF HUMAN P2Y<sub>1</sub>-LIKE G PROTEIN-COUPLED RECEPTOR

(57) Abstract: Reagents which regulate human P2Y<sub>1</sub>-like G protein-coupled receptor can play a role in preventing, ameliorating, or correcting dysfunctions or diseases including, but not limited to, infections such as bacterial, fungal, protozoan, and viral infections, particularly those caused by HIV viruses, pain, cancers, anorexia, bulimia, asthma, CNS diseases such as Parkinson's disease, acute heart failure, hypotension, hypertension, urinary retention, osteoporosis, diabetes, angina pectoris, myocardial infarction, ulcers, asthma, inflammation, allergies, multiple sclerosis, benign prostatic hypertrophy, and psychotic and neurological disorders, including anxiety, schizophrenia, manic depression, delirium, dementia, several mental retardation, and dyskinesias, such as Huntington's disease and Tourett's syndrome.



**WO 02/014511 A3**

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 01/09243

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C12N15/63 C12N1/19 C12N15/11 C12N15/62  
C07K14/705 C07K16/28 C12Q1/68 G01N33/68 A61K31/7088  
A61K38/17 A61K39/395 A61K48/00

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)

IPC 7 C12N C07K C12Q G01N 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)

EMBL, SEQUENCE SEARCH, EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE, CHEM ABS Dat

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                         | Relevant to claim No. |
|------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| X          | DATABASE EMBL [Online]<br>accession: AC026756,<br>24 March 2000 (2000-03-24)<br>ABOLA A P ET AL: "Homo sapiens chromosome<br>13 clone RP11-286P8, complete sequence."<br>XP002195810                                                                       | 1-4,<br>18-26         |
| X          | DATABASE EMBL [Online]<br>accession: AW827323,<br>23 May 2000 (2000-05-23)<br>NCI-CGAP: "hm31f01.x1 NCI CGAP Thy4 Homo<br>sapiens cDNA clone IMAGE:3014233 3'<br>similar to contains element MER17<br>repetitive element ;, mRNA sequence."<br>XP002195811 | 1-4,<br>18-26         |

☒ 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

"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

15 April 2002

Date of mailing of the international search report

02. 05. 2002

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Devijver, K

## INTERNATIONAL SEARCH REPORT

Intern. Application No

PCT/EP 01/09243

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                                                                                                                                                                                                                                                                                           | Relevant to claim No. |
|------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| E          | WO 01 87980 A (APPLERA CORP)<br>22 November 2001 (2001-11-22)<br>SEQ ID NO: 1; SEQ ID NO: 2; SEQ ID NO: 3<br>page 3; claims 1-23<br>---                                                                                                                                                                                                                                                                                                                                                                                      | 1-13,<br>15-67        |
| P,X        | WO 01 36471 A (ARENA PHARMACEUTICALS INC<br>;CHEN RUOPING (US); DANG HUONG T (US); L)<br>25 May 2001 (2001-05-25)<br>SEQ ID NO: 27; SEQ ID NO: 28<br>page 34; claims 1-80; examples 1-7<br>---                                                                                                                                                                                                                                                                                                                               | 1-13,<br>15-67        |
| E          | WO 01 87937 A (INCYTE GENOMICS INC<br>;KALLICK DEBORAH A (US); PATTERSON CHANDRA<br>(US) 22 November 2001 (2001-11-22)<br>SEQ ID NO: 2; SEQ ID NO: 10<br>claims 1-60; examples 1-18<br>---                                                                                                                                                                                                                                                                                                                                   | 1-13,<br>15-67        |
| P,X        | WO 01 57190 A (CAO YICHENG ;CHEN RUI HONG<br>(US); GOODRICH RYLE (US); HYSEQ INC (US)<br>9 August 2001 (2001-08-09)<br>SEQ ID NO: 975; SEQ ID NO: 1959<br>page 151; claims 1-28<br>page 184<br>-& DATABASE EMBL [Online]<br>accession: AAM79297,<br>6 November 2001 (2001-11-06)<br>TANG Y T ET AL: "Human protein SEQ ID NO<br>1959."<br>XP002195812<br>-& DATABASE EMBL [Online]<br>accession: AAK52430,<br>6 November 2001 (2001-11-06)<br>TANG Y T ET AL: "Human polynucleotide SEQ<br>ID NO 975."<br>XP002195813<br>--- | 1-13,<br>15-67        |
| E          | WO 01 66750 A (UPJOHN CO ;VOGELI GABRIEL<br>(US); WOOD LINDA S (US))<br>13 September 2001 (2001-09-13)<br>SEQ ID NO: 104<br>page 119; claims 1-95<br>---                                                                                                                                                                                                                                                                                                                                                                     | 1-13,<br>15-67        |
| P,X        | WO 01 49847 A (WHITE DAVID ;GLUCKSMANN<br>MARIA ALEXANDRA (US); MILLENNIUM PHARM<br>INC) 12 July 2001 (2001-07-12)<br>abstract; claims 1-26; figure 1<br>---                                                                                                                                                                                                                                                                                                                                                                 | 1-13,<br>15-67        |
| P,X        | WO 01 36473 A (PARODI LUIS A ;LIND PETER<br>(SE); SEJLITZ TORSTEN (SE); SCHELLIN KAT)<br>25 May 2001 (2001-05-25)<br>SEQ ID NO: 85; SEQ ID NO: 86<br>page 91; claims 1-97<br>---                                                                                                                                                                                                                                                                                                                                             | 1-13,<br>15-67        |
|            | ---                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                       |
|            | -/--                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                       |

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 01/09243

## 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        | <p>WO 01 57188 A (HYSEQ INC ;LIU CHENGHUA (US); TANG Y TOM (US); DRMANAC RADOJE T (U) 9 August 2001 (2001-08-09)<br/> page 106; claims 1-28<br/> SEQ ID NO: 1452<br/> page 144<br/> -&amp; DATABASE EMBL [Online]<br/> accession: ABB11082,<br/> 11 January 2002 (2002-01-11)<br/> TANG Y T ET AL: "Human P2Y purinoceptor homologue, SEQ ID NO:1452."<br/> XP002195814</p> | 1-13,<br>15-67        |
| A          | <p>---<br/> AYYANATHAN KASIRAJAN ET AL: "Cloning and chromosomal localization of the human P2Y1 purinoceptor."<br/> BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS,<br/> vol. 218, no. 3, 1996, pages 783-788,<br/> XP002195807<br/> ISSN: 0006-291X</p>                                                                                                               |                       |
| A          | <p>---<br/> DATABASE EMBL [Online]<br/> accession: AJ006945,<br/> 16 October 1998 (1998-10-16)<br/> LEON C: "Human P2Y1 gene"<br/> XP002195815</p>                                                                                                                                                                                                                          |                       |
| A          | <p>---<br/> KUNAPULI SATYA P ET AL: "P2 receptor subtypes in the cardiovascular system."<br/> BIOCHEMICAL JOURNAL,<br/> vol. 336, no. 3,<br/> 15 December 1998 (1998-12-15), pages<br/> 513-523, XP002195808<br/> ISSN: 0264-6021</p>                                                                                                                                       |                       |
| A          | <p>---<br/> BARNARD ERIC A ET AL: "G protein-coupled receptors for ATP and other nucleotides: A new receptor family."<br/> TRENDS IN PHARMACOLOGICAL SCIENCES,<br/> vol. 15, no. 3, 1994, pages 67-70,<br/> XP002195809<br/> ISSN: 0165-6147<br/> cited in the application<br/> -----</p>                                                                                   |                       |

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP 01/09243

### Box I Observations where certain claims were found unsearchable (Continuation of item 1 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:  
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.: 14,68-71; in part: 8,9,13,15-17,33,52,53,55,58-60,62  
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:  
see FURTHER INFORMATION sheet PCT/ISA/210
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 II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

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

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
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.:

#### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box I.1

Although claims 54, 56 and 57 (completely) and claims 13, 16, 17, 52, 53, 55 and 59 (in part) are directed to a method of treatment of the human/animal body (as far as in vivo methods are concerned), the search has been carried out and based on the alleged effects of the compound/composition.

## Continuation of Box I.2

Claims Nos.: 14, 68-71; in part: 8, 9, 13, 15-17, 33, 52, 53, 55, 58-60, 62

Claims 8 and 9 refer to a reagent which specifically interacts with the polynucleotide of claim 1 or a P2Y1-like GPCR polypeptide of claim 4 without giving a true technical characterization. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds, namely: antibodies which specifically bind to a polypeptide of claim 4 and antisense (complementary) oligonucleotides of claim 1. In consequence, the scope of said claims is ambiguous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 5 and 6 PCT). An attempt is made to define the compound by reference to a result to be achieved.

This lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to: antibodies which specifically bind to a polypeptide of claim 4 and antisense (complementary) oligonucleotides of claim 1.

Claim 13 refers to a reagent which specifically binds to any polynucleotide of claim 1 or any P2Y1-like GPCR polypeptide of claim 4 without giving a true technical characterization. The claim covers all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds, namely: antibodies which specifically bind to a polypeptide of claim 4, antisense (complementary) oligonucleotides of claim 1 and ribozymes. In consequence, the scope of said claim is ambiguous and vague, and its subject-matter is not sufficiently disclosed and supported (Art. 5 and 6 PCT). An attempt is made to define the compound by reference to a result to be achieved.

This lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claim which appear to be clear, supported and disclosed, namely those parts relating to: antibodies which specifically bind to a polypeptide of claim 4, antisense (complementary) oligonucleotides of claim 1 and ribozymes.

The above comment also applies for claims 33, 52, 53, 55, 58-60, 62.

Claim 14 refers to a reagent that modulates the activity of a P2Y1-like GPCR polypeptide of claim 4 or polynucleotide of claim 1 without giving a

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

true technical characterization. Moreover, no such compounds are defined in the application. In consequence, the scope of said claim is ambiguous and vague, and its subject-matter is not sufficiently disclosed and supported (Art. 5 and 6 PCT).

No meaningful search can be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the results to be achieved.

The above comment also applies for claims 15-17, 68-71.

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/EP 01/09243

| Patent document<br>cited in search report |   | Publication<br>date | Patent family<br>member(s)                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Publication<br>date                                                                                                                                                                                                                                                                                                                                                                                                |
|-------------------------------------------|---|---------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| WO 0187980                                | A | 22-11-2001          | AU 6171501 A<br>WO 0187980 A2                                                                                                                                                                                                                                                                                                                                                                                                                                              | 26-11-2001<br>22-11-2001                                                                                                                                                                                                                                                                                                                                                                                           |
| WO 0136471                                | A | 25-05-2001          | AU 1769601 A<br>WO 0136471 A2                                                                                                                                                                                                                                                                                                                                                                                                                                              | 30-05-2001<br>25-05-2001                                                                                                                                                                                                                                                                                                                                                                                           |
| WO 0187937                                | A | 22-11-2001          | AU 6472101 A<br>WO 0187937 A2<br>AU 6181401 A<br>WO 0190359 A2                                                                                                                                                                                                                                                                                                                                                                                                             | 26-11-2001<br>22-11-2001<br>03-12-2001<br>29-11-2001                                                                                                                                                                                                                                                                                                                                                               |
| WO 0157190                                | A | 09-08-2001          | AU 2591801 A<br>AU 3128801 A<br>AU 3297101 A<br>AU 3300301 A<br>AU 3329301 A<br>AU 3484701 A<br>AU 3484801 A<br>AU 3486501 A<br>AU 3494401 A<br>AU 3665801 A<br>AU 3666001 A<br>AU 3666301 A<br>AU 3672101 A<br>AU 4314201 A<br>WO 0153326 A1<br>WO 0155334 A2<br>WO 0155335 A2<br>WO 0157255 A1<br>WO 0157260 A1<br>WO 0157175 A2<br>WO 0157261 A1<br>WO 0157262 A1<br>WO 0157187 A2<br>WO 0157265 A1<br>WO 0157188 A2<br>WO 0157266 A1<br>WO 0157267 A1<br>WO 0157190 A2 | 31-07-2001<br>14-08-2001<br>07-08-2001<br>07-08-2001<br>14-08-2001<br>14-08-2001<br>14-08-2001<br>14-08-2001<br>14-08-2001<br>14-08-2001<br>14-08-2001<br>14-08-2001<br>14-08-2001<br>14-08-2001<br>14-08-2001<br>26-07-2001<br>02-08-2001<br>02-08-2001<br>09-08-2001<br>09-08-2001<br>09-08-2001<br>09-08-2001<br>09-08-2001<br>09-08-2001<br>09-08-2001<br>09-08-2001<br>09-08-2001<br>09-08-2001<br>09-08-2001 |
| WO 0166750                                | A | 13-09-2001          | AU 4009701 A<br>WO 0166750 A2                                                                                                                                                                                                                                                                                                                                                                                                                                              | 17-09-2001<br>13-09-2001                                                                                                                                                                                                                                                                                                                                                                                           |
| WO 0149847                                | A | 12-07-2001          | AU 2458101 A<br>WO 0149847 A2                                                                                                                                                                                                                                                                                                                                                                                                                                              | 16-07-2001<br>12-07-2001                                                                                                                                                                                                                                                                                                                                                                                           |
| WO 0136473                                | A | 25-05-2001          | AU 1617801 A<br>WO 0136473 A2                                                                                                                                                                                                                                                                                                                                                                                                                                              | 30-05-2001<br>25-05-2001                                                                                                                                                                                                                                                                                                                                                                                           |
| WO 0157188                                | A | 09-08-2001          | AU 2591801 A<br>AU 3128801 A<br>AU 3297101 A<br>AU 3300301 A<br>AU 3329301 A<br>AU 3484701 A<br>AU 3484801 A<br>AU 3486501 A<br>AU 3494401 A                                                                                                                                                                                                                                                                                                                               | 31-07-2001<br>14-08-2001<br>07-08-2001<br>07-08-2001<br>14-08-2001<br>14-08-2001<br>14-08-2001<br>14-08-2001<br>14-08-2001                                                                                                                                                                                                                                                                                         |

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 01/09243

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
|-------------------------------------------|---------------------|----------------------------|---------------------|
| WO 0157188                                | A                   | AU 3665801 A               | 14-08-2001          |
|                                           |                     | AU 3666001 A               | 14-08-2001          |
|                                           |                     | AU 3666301 A               | 14-08-2001          |
|                                           |                     | AU 3672101 A               | 14-08-2001          |
|                                           |                     | AU 4314201 A               | 14-08-2001          |
|                                           |                     | WO 0153326 A1              | 26-07-2001          |
|                                           |                     | WO 0155334 A2              | 02-08-2001          |
|                                           |                     | WO 0155335 A2              | 02-08-2001          |
|                                           |                     | WO 0157255 A1              | 09-08-2001          |
|                                           |                     | WO 0157260 A1              | 09-08-2001          |
|                                           |                     | WO 0157175 A2              | 09-08-2001          |
|                                           |                     | WO 0157261 A1              | 09-08-2001          |
|                                           |                     | WO 0157262 A1              | 09-08-2001          |
|                                           |                     | WO 0157187 A2              | 09-08-2001          |
|                                           |                     | WO 0157265 A1              | 09-08-2001          |
|                                           |                     | WO 0157188 A2              | 09-08-2001          |
|                                           |                     | WO 0157266 A1              | 09-08-2001          |
|                                           |                     | WO 0157267 A1              | 09-08-2001          |
|                                           |                     | WO 0157190 A2              | 09-08-2001          |
| -----                                     |                     |                            |                     |