

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
07 December 2017 (07.12.2017)



(10) International Publication Number
WO 2017/208253 A9

(51) International Patent Classification:
C07D 215/56 (2006.01)

TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
KM, ML, MR, NE, SN, TD, TG).

(21) International Application Number:
PCT/IN2017/050203

Declarations under Rule 4.17:

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
- *of inventorship (Rule 4.17(iv))*

(22) International Filing Date:
26 May 2017 (26.05.2017)

Published:

- *with international search report (Art. 21(3))*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
201611018491 30 May 2016 (30.05.2016) IN

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(88) Date of publication of the international search report:
04 January 2018 (04.01.2018)

Date of publication of the revised international search report:

15 March 2018 (15.03.2018)

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(15) Information about Correction:
see Notice of 15 March 2018 (15.03.2018)

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,

(54) Title: AN IMPROVED PROCESS FOR THE SYNTHESIS OF IVACAFTOR

(57) Abstract: The present disclosed an improved process for the synthesis of ivacaftor starting from indole acetic acid ester which can be performed in batch as well as continuous flow synthesis. The present invention further disclosed to a continuous process for the synthesis of compound of formula (II) or formula (III) from compound of formula (I) in continuous flow reactor.

INTERNATIONAL SEARCH REPORT

RE-ISSUED VERSION

International application No

PCT/IN2017/050203

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D215/56
ADD.

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)

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 practicable, search terms used)

EP0-Internal, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	N. VASUDEVAN ET AL: "Breaking and Making of Rings: A Method for the Preparation of 4-Quinolone-3-carb-oxylic Acid Amides and the Expensive Drug Ivacaftor", EUROPEAN JOURNAL OF ORGANIC CHEMISTRY, 3 November 2015 (2015-11-03), pages n/a-n/a, XP055237434, DE ISSN: 1434-193X, DOI: 10.1002/ejoc.201501048 schemes 1, 2 and 3 -----	1-9
A	WO 2007/079139 A2 (VERTEX PHARMA [US]; HURTER PATRICIA [US]) 12 July 2007 (2007-07-12) page 46, paragraph 212 - page 47, paragraph 219 -----	1-9



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 application or patent 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

26 September 2017

Date of mailing of the international search report

31/01/2018

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IN2017/050203

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 all searchable 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.:

1-9

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: 1-9

A process for the synthesis of ivacaftor.

2. claims: 10-14

A process for the synthesis of a compound of formula (II) or (III).

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IN2017/050203

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2007079139	A2	12-07-2007	
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		US 2017231970 A1	17-08-2017
		WO 2007079139 A2	12-07-2007