



(43) International Publication Date
23 June 2016 (23.06.2016)

(10) International Publication Number
WO 2016/100677 A3

(51) International Patent Classification:

A61K 9/00 (2006.01) A61K 47/26 (2006.01)
A61K 47/10 (2006.01) A61K 31/00 (2006.01)

(21) International Application Number:

PCT/US2015/066396

(22) International Filing Date:

17 December 2015 (17.12.2015)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/093,801 18 December 2014 (18.12.2014) US

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

Declarations under Rule 4.17:

- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))
- of inventorship (Rule 4.17(iv))

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))

(88) Date of publication of the international search report:

11 August 2016

(54) Title: PHARMACEUTICAL FORMULATIONS OF TROPOMYOSIN RELATED KINASE (TRK) INHIBITORS

(57) Abstract: Pharmaceutical formulations with a tropomyosin-related kinase inhibitor ("Trk inhibitor") are disclosed. The pharmaceutical formulations comprise 3-(3-methoxy-4-((4-methoxybenzyl)oxy)benzyl)-6-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridin-2-amine in microcrystalline suspension formulations in its monohydrate form, which shows improved characteristics over the anhydrate form, and in extended release formulations. The extended release pharmaceutical formulations comprise 3-(3-methoxy-4-((4-methoxybenzyl)oxy)benzyl)-6-(1-methyl-1H-pyrazol-4-yl)-3H-imidazo[4,5-b]pyridin-2-amine-loaded microspheres.



WO 2016/100677 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2015/066396

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K9/00 A61K47/10 A61K47/26 A61K31/00
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)

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 practicable, search terms used)

EPO-Internal, EMBASE, 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	US 2010/204246 A1 (DAVIES AUDREY [US] ET AL) 12 August 2010 (2010-08-12) paragraphs [0156] - [0175], [0201] - [0207], [0214] - [0306] claims; examples -----	1-118
A	WO 2013/176970 A1 (MERCK SHARP & DOHME [US]; STACHEL SHAWN J [US]; EGBERTSON MELISSA [US]) 28 November 2013 (2013-11-28) the whole document -----	1-20
A,P	WO 2015/089139 A1 (GENZYME CORP [US]; KANE JOHN L [US]; MATTHEWS GLORIA [US]; METZ MARKUS) 18 June 2015 (2015-06-18) the whole document -----	1-118



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

13 June 2016

Date of mailing of the international search report

21/06/2016

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2015/066396

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.:

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2015/066396

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2010204246 A1	12-08-2010	CN 101679429 A EP 2155742 A1 JP 2010524911 A US 2010204246 A1 WO 2008129255 A1	24-03-2010 24-02-2010 22-07-2010 12-08-2010 30-10-2008
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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-20

GZ389988 pharmaceutical composition comprising acceptable excipient such as diluent, suspending agent and buffering agent

2. claims: 21-55

Extended release pharmaceutical formulation of GZ389988 amine-loaded microspheres

3. claims: 56-60

preparation process of a crystalline form of GZ389988A

4. claims: 61-65

preparation process of a monohydrate form of GZ389988A

5. claims: 66-76

preparation process of a amine-loaded microcapsule of GZ389988

6. claims: 77-87

reparation process of a amine-loaded microcapsule of GZ389988A by solvent extraction and to form a drug suspension

7. claims: 88-103

preparation process of a amine-loaded microcapsule of GZ389988A amine-loaded microcapsule by spray drying to form a drug solution

8. claims: 104-118

preparation process of a amine-loaded microcapsule of GZ389988A amine-loaded microcapsule by spray drying to form a drug suspension
