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(71) Applicant (for all designated States except US): **NOVARTIS AG** [CH/CH]; Lichtstrasse 35, CH-4056 Basel (CH).

(72) Inventors; and

(71) Applicants (for US only): **GRAUS PORTA, Diana** [ES/CH]; c/o Novartis Pharma AG, Klybeckstrasse 141, CH-4057 Basel (CH). **WOEHRLE, Simon** [DE/CH]; c/o Novartis Pharma AG, Klybeckstrasse 141, CH-4057 Basel (CH).

(74) Agent: **PFISTER-FU, Yixin**; Novartis Pharma AG, Postfach, CH-4057 Basel (CH).

(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, LT, 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.

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Declarations under Rule 4.17:

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

[Continued on next page]

(54) Title: FGF-R TYROSINE KINASE ACTIVITY INHIBITORS - USE IN DISEASES ASSOCIATED WITH LACK OF OR REDUCED SNF5 ACTIVITY

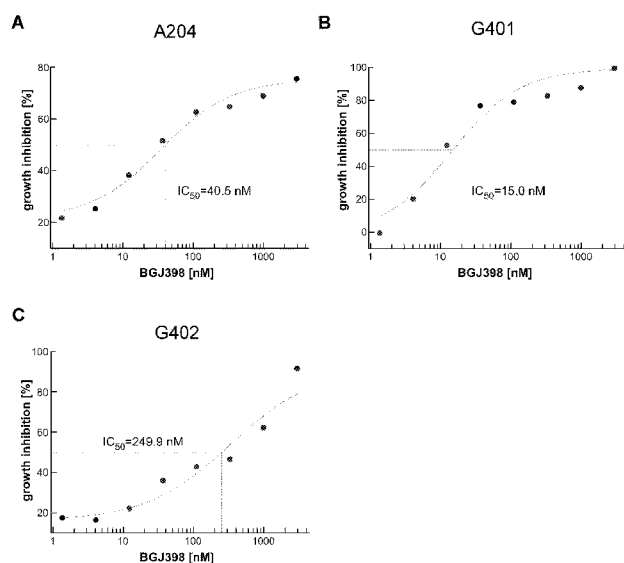


Figure 1

(57) Abstract: FGF-R tyrosine Kinase Activity Inhibitors useful in Case of Lack of SNF5 Activity. The invention relates to the use of FGF-R inhibitors in the (prophylactic and/or therapeutic) treatment of proliferative diseases that depend on at least partial lack of SNF5 activity, the use of said inhibitors for the preparation of a pharmaceutical composition (medicament) for said use, said inhibitors for use in a method of (therapeutic and/or prophylactic) treatment of a proliferative disease depends on at least partial lack of SNF5 activity, a method of (prophylactic and/or therapeutic) treatment of a proliferative disease that depends on at least partial lack of SNF5 activity and a pharmaceutical composition (medicament) for use in the (prophylactic and/or therapeutic) treatment of a proliferative disease that depends on at least partial lack of SNF5 activity, as well as related invention embodiments.



**Published:**

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

- *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))*

4 December 2014

# INTERNATIONAL SEARCH REPORT

International application No PCT/IB2014/060087
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<b>A. CLASSIFICATION OF SUBJECT MATTER</b> INV. A61K39/395 A61K31/496 A61K31/506 A61K31/519 A61K31/713 G01N33/00 A61P35/00 ADD. According to International Patent Classification (IPC) or to both national classification and IPC				
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) A61K G01N 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, WPI Data, BEILSTEIN Data, BIOSIS, EMBASE, CHEM ABS Data				
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>				
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
X	LOCH DAVID C ET AL: "Lineage-Specific Biomarkers Predict Response to FGFR Inhibition", CANCER DISCOVERY, vol. 2, no. 12, December 2012 (2012-12), pages 1081-1083, XP002726889, page 1081, right-hand column, paragraph 2nd <p style="text-align: center;">----- -/--</p>	1,2,5-12		
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <span style="margin-left: 200px;"><input type="checkbox"/> See patent family annex.</span>				
* Special categories of cited documents : <table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none; vertical-align: top;">                     "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                 </td> <td style="width: 50%; border: none; vertical-align: top;">                     "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                      "&amp;" document member of the same patent family                 </td> </tr> </table>			"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
"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	Date of mailing of the international search report			
10 July 2014	25/09/2014			
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer  Opravz, Petra			

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IB2014/060087

## 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.:

8(completely); 1-7, 9-12(partially)

### 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

International application No  
PCT/IB2014/060087

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>KONECNY GOTTFRIED E ET AL: "Activity of the Fibroblast Growth Factor Receptor Inhibitors Dovitinib (TKI258) and NVP-BGJ398 in Human Endometrial Cancer Cells", MOLECULAR CANCER THERAPEUTICS, vol. 12, no. 5, 26 February 2013 (2013-02-26), pages 632-642, XP002726890, abstract</p> <p>-----</p>	1,2,5-7, 9,10
X,P	<p>WÖHRLE SIMON ET AL: "Fibroblast growth factor receptors as novel therapeutic targets in SNF5-deleted malignant rhabdoid tumors.", PLOS ONE, vol. 8, no. 10, E77652, 30 October 2013 (2013-10-30), pages 1-11, XP002726891, ISSN: 1932-6203, DOI: 10.1371/journal.pone.0077652 the whole document</p> <p>-----</p>	1-12
A	<p>KLENKE F M ET AL: "Tyrosine kinase inhibitor SU6668 represses chondrosarcoma growth via antiangiogenesis in vivo", BMC CANCER, vol. 7, 17 March 2007 (2007-03-17), XP002123128, ISSN: 1471-2407 abstract</p> <p>-----</p>	1
T	<p>Anonymous: "Final report: Therapeutically targeting aberrant chromatin remodeling in sarcomas (Project Number: SFA09-20)", Sarcoma Foundation of America</p> <p>1 February 2011 (2011-02-01), XP002726892, Retrieved from the Internet: URL:<a href="http://www.curesarcoma.org/documents/uploads/Roberts_Final_Report.pdf">http://www.curesarcoma.org/documents/uploads/Roberts_Final_Report.pdf</a> [retrieved on 2014-07-09] page 3, last paragraph - page 4, paragraph first</p> <p>-----</p>	

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

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

1. claims: 8(completely); 1-7, 9-12(partially)

An FGFR inhibitor, i.e. BGJ398, or a pharmaceutically acceptable salt thereof for use in a therapeutically effective amount treating a disease associated with at least partial lack of SNF5 activity.

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2. claims: 1-7, 9-12(all partially)

An FGFR inhibitor, i.e. AZD-4547, or a pharmaceutically acceptable salt thereof for use in a therapeutically effective amount treating a disease associated with at least partial lack of SNF5 activity.

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3. claims: 1-7, 9-12(all partially)

An FGFR inhibitor, i.e. TKI258, or a pharmaceutically acceptable salt thereof for use in a therapeutically effective amount treating a disease associated with at least partial lack of SNF5 activity.

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4. claims: 1-6, 9-12(all partially)

An FGFR inhibiting antibody or a pharmaceutically acceptable salt thereof for use in a therapeutically effective amount treating a disease associated with at least partial lack of SNF5 activity.

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5. claims: 1-6, 9-12(all partially)

An siRNA of FGFR or a pharmaceutically acceptable salt thereof for use in a therapeutically effective amount treating a disease associated with at least partial lack of SNF5 activity.

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6. claim: 13

Method for determining whether a patient is sensitive to an FGFR inhibitor treatment, comprising the steps of  
a) determining whether said patient at least partially lacks of SNF5 activity by qRT-PCR, immunoblotting, sequencing or other mutation detecting methods;  
where  
b) if a) is affirmative, then said patient is sensitive to an FGFR inhibitor treatment.

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