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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,  
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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 applicant's entitlement to apply for and be granted a  
patent (Rule 4.17(ii))*
- *as to the applicant's entitlement to claim the priority of the  
earlier application (Rule 4.17(iii))*

**Published:**

- *with international search report (Art. 21(3))*

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

17 March 2016

(54) **Title:** SMALL MOLECULE INHIBITORS OF G PROTEIN COUPLED RECEPTOR 6 KINASES POLYPEPTIDES

(57) **Abstract:** This document relates to inhibitors of G protein coupled receptor 6 kinase (GRK6) polypeptides as well as methods and materials for using such inhibitors to treat hematological malignancies, inflammation diseases, and autoimmune disorders.



## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 15/26926

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C07D 405/04; C07D 405/14; C07D 249/12 (2015.01)

CPC - C07D 249/12; A61K 31/4196; C07D 405/02; C07D 407/14

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(8): C07D 405/04; C07D 405/14; C07D 249/12 (2015.01)

CPC: C07D 249/12; A61K 31/4196; C07D 405/02; C07D 407/14

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
USPC: 514/382; 514/384; 514/461; 514/562; 514/564

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PatBase, Google Scholar, PubWEST, PubChem

G-protein coupled receptor 6 kinase, GRK6, inhibitor, 5-methylfuran-2-yl, pyrazole, thioacetic acid, sulfanylacetic acid

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                         | Relevant to claim No. |
|-----------|------------------------------------------------------------------------------------------------------------|-----------------------|
| Y         | WO 2013/063458 A2 (STEWART et al.) 02 May 2013 (02.05.2013) pg 1, ln 25 to pg 2, ln 3; pg 13               | 1, 5-6, 17-20         |
| Y         | US 7,226,941 B2 (PARK et al.) 05 June 2007 (05.06.2007) col 1, ln 15-19; col 16, ln 38-45                  | 1, 5-6, 17-20         |
| Y         | US 2005/0288347 A1 (HODGE et al.) 29 December 2005 (29.12.2005) para [0207], [0211], Table 3, pg 34, pg 59 | 1, 5-6                |
| A         | US 2010/0099683 A1 (TOMKINSON et al.) 22 April 2010 (22.04.2010) Table 2, Compound 42                      | 1, 5-6, 17-20         |

☐ Further documents are listed in the continuation of Box C.

\* 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

"&amp;" document member of the same patent family

Date of the actual completion of the international search

24 September 2015 (24.09.2015)

Date of mailing of the international search report

19 OCT 2015

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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 15/26926

## 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.: 51-66  
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:  
--Please see attached 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 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, 5-6 and 17-20

### 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.

## Attachment to Box.No.III:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Group I+: Claims 1-50 directed to a compound of Formula I, represented by Formula IA, IB, II, IIA, III or IIIA. The compound of Formula I will be searched to the extent that the compound encompasses the first species of claim 1, wherein

X is CH; Z is -C(O)OR<sub>1</sub>, where R<sub>1</sub> is H;

R<sub>2</sub> is a substituted C<sub>1</sub>-alkyl;

R<sub>3</sub> and R<sub>4</sub> are each H; and

m is an integer 1.

It is believed that claims 1, 5-6 and 17-20 encompass this first named invention, and thus these claims will be searched without fee to the extent that they encompass the first species of claim 1.

Applicant is invited to elect additional compounds of Formula I, wherein each additional compound elected will require one additional invention fee. Applicants must specify the claims that encompass any additionally elected compound. Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched.

An exemplary election would be a compound of claim 1, wherein

X is N; Z is -C(O)OR<sub>1</sub>, where R<sub>1</sub> is H;

R<sub>2</sub> is an unsubstituted phenyl;

R<sub>3</sub> and R<sub>4</sub> are each H; and

m is an integer 1 (i.e., claims 1-3, 11-12, 14, 16).

The group of inventions listed above does not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Each invention within Group I+ includes the technical feature of a unique compound of Formula I, which is not required in any other invention of the group.

The inventions of Groups I+ share the technical feature of a compound having the core structure of Formula I.

This shared technical feature, however, does not provide a contribution over the prior art as being anticipated by PubChem-CID-43164245 (Create Date: 21 July 2009) (hereinafter 'PubChem').

PubChem discloses a compound of Formula I, wherein X is N; m is 1 and Z is COOR<sub>1</sub>, where R<sub>1</sub> is H; R<sub>2</sub> is C<sub>1</sub>-alkyl and wherein R<sub>3</sub> and R<sub>4</sub> are each H (pg 3, Fig), wherein said compound has a heteroaryl-1,2,4-triazole-thioacetic acid core structure (pg 3, Fig).

As said compound was known in the art at the time of the invention, this cannot be considered a special technical feature, that would otherwise unify the inventions of Group I+.

The inventions of Group I+, therefore, lack unity under PCT Rule 13.

Note reg. item 4: Claims 51-66 are unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). These claims are, therefore, not included in the above analysis.