

- (51) International Patent Classification:

A61K 31/395 (2006.01) A61K 31/13 (2006.01)

A61K 31/505 (2006.01) A61K 31/33 (2006.01)
- (21) International Application Number:

PCT/US2024/032272
- (22) International Filing Date:

03 June 2024 (03.06.2024)
- (25) Filing Language:

English
- (26) Publication Language:

English
- (30) Priority Data:

63/505,969 02 June 2023 (02.06.2023) US

63/618,980 09 January 2024 (09.01.2024) US
- (71) Applicant: ATOMWISE INC. [US/US]; 717 Market Street, Suite 800, San Francisco, CA 94103 (US).
- (72) Inventor: MORTEZAEI, Shahab; c/o Atomwise Inc., 717 Market Street, Suite 800, San Francisco, CA 94103 (US).
- (74) Agent: MANN, Jeffrey, S. et al.; Morgan, Lewis & Bockius LLP, One Market, Spear Street Tower, San Francisco, CA 94105 (US).
- (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, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, MG, MK, MN, MU, 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, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, 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, ME, 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).
- (54) Title: INHIBITORS OF TYK2
- (57) Abstract: In exemplary embodiments, inhibitors of Tyrosine Kinase 2 (TYK2), pharmaceutical formulations comprising these compounds, methods of using these compounds to inhibit TYK2, and treat diseases such as autoimmune and inflammatory diseases are provided.



WO 2024/250010 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 24/32272

A. CLASSIFICATION OF SUBJECT MATTER

IPC - INV. A61K 31/395, A61K 31/505, A61K 31/13 (2024.01)

ADD. A61K 31/33 (2024.01)

CPC - INV. A61K 31/395, A61K 31/505, A61K 31/13

ADD. A61K 31/33

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)

See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

See Search History document

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

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2020/0317705 A1 (ARIAD Pharmaceuticals, Inc.), 08 October 2020 (08.10.2020), entire document, especially para[0005]-[0025]	1
A	US 2012/0329784 A1 (Kallander et al.), 27 December 2012 (27.12.2012), entire document, especially para[0005]-[0016]	1
A	US 2010/0010025 A1 (Duthaler et al.), 14 January 2010 (14.01.2010), entire document, especially para[0002]-[0005], [0019]	1
A	US 10,730,860 B2 (Dana-Farber Cancer Institute, Inc.), 04 August 2020 (04.08.2020), entire document, especially col 33, ln 48-67; col 34, ln 1-67; col 35, ln 1-56	1
A	"Pubchem CID 151736710", Create date: 13 August 2020 (13.08.2020), entire document, especially page 2, compound listed	1
A	WO 2011/088027 A1 (Kallander et al.), 21 July 2011 (21.07.2011), entire document, especially page 2-3	1



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

"D" document cited by the applicant in the international application

"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

25 July 2024

Date of mailing of the international search report

OCT 16 2024

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-8300

Authorized officer

Kari Rodriguez

Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 24/32272

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.: 5-11, 14, 16-24
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 supplemental box---

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

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/US 24/32272

Box III: lack of unity

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. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I+: Claims 1-4, 12-13, 15, and 25 are directed to a compound having a structure of Formula I as seen in instant claim 1. Claim 1 will be searched to the extent that it encompasses the first species of claim 1, represented by a compound of Formula I wherein X1 is N; X and X2 are independently N; R2 is the first structure listed wherein R5 is C1 alkyl; X3 is N; X4 is N; X5 is N; wherein when neither R7 and R8 nor R8 and R9, together with the carbons to which they are attached, are joined to form a ring not more than one member selected from R7, R8 and R9 is other than H; R9 does not comprise the moiety as listed in instant claim 1; and when at least one member selected from R7, R8 and R9 is Me, R2 is the structure listed in instant claim 1. It is believed that claim 1 read on this first named invention, and thus these claims will be searched without fee. This first named invention has been selected based on the guidance set forth in section 10.54 of the PCT International Search and Preliminary Examination Guidelines. Applicant is invited to elect additional compounds of claim 1, 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. Additionally, an exemplary election wherein different actual variables are selected is suggested. An exemplary election would be a compound of Formula I wherein X1 is N; X and X2 are independently N; R2 is the first structure listed wherein R5 is C2 alkyl; X3 is N; X4 is N; X5 is N; wherein when neither R7 and R8 nor R8 and R9, together with the carbons to which they are attached, are joined to form a ring not more than one member selected from R7, R8 and R9 is other than H; R9 does not comprise the moiety as listed in instant claim 1; and when at least one member selected from R7, R8 and R9 is Me, R2 is the structure listed in instant claim 1 (i.e., claim 1).

The groups of inventions listed above do 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:

Special Technical Features:

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

Common Technical Features:

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

These shared technical features, however, do not provide a contribution over the prior art as being obvious over US 2012/0329784 A1 to Kallander et al. (hereinafter 'Kallander') in view of a document entitled "Pubchem CID 151736710" (hereinafter 'Pubchem-710'). Kallander teaches a compound analogous to a compound of Formula I as seen in instant claim 1 wherein X1 is CR1 wherein R1 is H; X and X2 are independently CH; R2 is -S(O)2-R5 wherein R5 is C1 alkyl; X3 is CR7; X4 is CR8; X5 is CR9; R7 is H; R8 is substituted C1 alkyl; R9 is H; wherein when neither R7 and R8 nor R8 and R9, together with the carbons to which they are attached, are joined to form a ring not more than one member selected from R7, R8 and R9 is other than H; R9 does not comprise the moiety as listed in instant claim 1; and when at least one member selected from R7, R8 and R9 is Me, R2 is the structure listed in instant claim 1 (see para[0686]; see Example 306) but does not teach wherein the carbon para to R2 is unsubstituted. However, Pubchem-710 does teach a compound analogous to a compound of Formula I wherein the carbon para to R2 is unsubstituted (see page 2, compound listed). Therefore, based on the structural similarities between the two compounds, it would have been obvious to a person of ordinary skill in the art to combine these references and replace the substituent para to R2 (i.e., -S(O)2-NH-CH3) of Kallander's compound with a hydrogen substitution as taught by Pubchem-710 in order to isolate all possible derivatives of Kallander's compounds by routine experimentation.

Accordingly, the inventions listed as Groups I+ above lack unity of invention under PCT Rule 13 because they do not share a same or corresponding special technical feature providing contribution over prior art.

RE: Item 4: Claims 5-11, 14, and 16-24 have been held unsearchable because they are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Claim 1 lacks clarity. R10 is listed as a variable. However, R10 is not incorporated anywhere in Formula I as seen in instant claim 1. For the purposes of this opinion, R10 will be disregarded.