



(51) International Patent Classification:

A61K 39/395 (2006.01) C07K 16/46 (2006.01)
C07K 16/28 (2006.01) C12N 5/078 (2010.01)

(21) International Application Number:

PCT/US2017/025951

(22) International Filing Date:

04 April 2017 (04.04.2017)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/317,906 04 April 2016 (04.04.2016) US

(72) Inventor; and

(71) Applicant: SANDLER, Vladislav [US/US]; 320 West 83rd Street, Apartment 6A, New York, NY 10024 (US).

(74) Agent: LUBIT, Beverly, W.; Chiesa Shahinian & Giantomasi PC, One Boland Drive, West Orange, NJ 07052 (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, 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, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

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:

16 November 2017 (16.11.2017)

(54) Title: METHOD OF ELIMINATING HEMATOPOIETIC STEM CELLS/HEMATOPOIETIC PROGENITORS (HSC/HP) IN A PATIENT USING BI-SPECIFIC ANTIBODIES

FIG. 1A

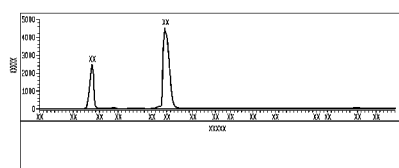


FIG. 1B

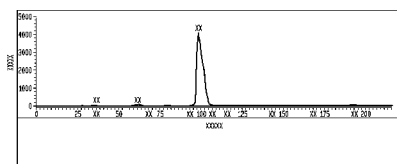
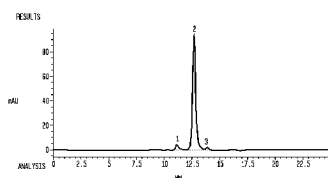


FIG. 1C



(57) Abstract: The described invention provides compositions containing bi-specific antibodies that bind to human tyrosine kinase receptor FLT3/FLK2 receptor protein and to CD3 receptor protein expressed on T-cells and use of the compositions containing the bispecific antibodies in the preparation of a medicament for eliminating hematopoietic stem cells/hematopoietic progenitors (HSC/HP) in a patient.



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US17/25951

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61K 39/395; C07K 16/28, 16/46; C12N 5/078 (2017.01)

CPC - A61K 39/001, 39/395; C07K 16/28, 16/2809, 16/468; C12N 5/0634

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 --- Y	US 2015/0119555 A1 (SYNIMMUNE GMBH) 30 April 2015; paragraphs [0011], [0020], [0058], [0061], [0084], [0096], [0170]; Figures 6A1 and 6B.	10, 11 ----- 1, 3, 4-9
Y	US 2012/0328612 A1 (GROSSE-HOVEST, et al.) 27 December 2012; paragraphs [0004], [0022], [0024], [0025], [0027], [0058], [0097], [0123], [0128], [0141], [0200], [0206], [0207], [0215], [0220], [0246], [0268], [0269]; Figure 13A	1, 3, 4-9
A	WO 2016/023909 A1 (DEUTSCHES KREBSFORSCHUNG-SZENTRUM, et al.) 18 February 2016; paragraph [0098]	2, 12

☐ 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 September 2017 (13.09.2017)

Date of mailing of the international search report

04 OCT 2017

Name and mailing address of the ISA/

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

Facsimile No. 571-273-8300

Authorized officer

Shane Thomas

PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US17/25951

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:

-Please see supplemental page-

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.:
Claims 1-12

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/US17/25951

-Continued from Box No. III: Observations where unity of invention is lacking-

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 examined, the appropriate additional examination fees must be paid.

Group I, Claims 1-12 are directed toward a bi-specific antibody that binds to human FLT3 and CD3; a method for preparing the antibody; and a method for preparing or conditioning a patient therewith.

Groups II+, Claims 13-28 and SEQ ID NOs: 5 and 7 are directed toward a monoclonal antibody or antigen binding fragment thereof that binds to human FLT3/FLK2.

The monoclonal antibody can be searched to the extent that it comprises a light chain encompassing SEQ ID NO: 5 (first exemplary light chain); and a heavy chain encompassing SEQ ID NO: 7 (first exemplary heavy chain). Applicant is invited to elect additional pair(s) of light and heavy chain sequence(s), with specified SEQ ID NO: for each, to be searched. Additional pair(s) of light and heavy chain sequence(s) can be searched upon the payment of additional fees. It is believed that claims 13-16 encompass this first named invention of Groups (II)+ and thus these claims can be searched with payment of a fee for the search of Groups (II)+, to the extent that they encompass SEQ ID NO: 5 (light chain); and SEQ ID NO: 7 (heavy chain). Applicants must specify the claims that encompass any additionally elected pair(s) of light and heavy chain sequence(s). Applicants must further indicate, if applicable, the claims which encompass the first named invention of Groups (II)+, 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) can result in only the first claimed invention of groups (II)+ to be searched/examined. An exemplary election would be a light chain encompassing SEQ ID NO: 9 (first exemplary elected light chain) and a heavy chain encompassing SEQ ID NO: 11 (first exemplary elected heavy chain).

The inventions listed as Groups I and II+ 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: the special technical features of Group I include a bi-specific antibody that binds to CD3, not present in any of Groups II+; the special technical features of Groups II+ include SEQ ID NO: 5, not present in Group I.

No technical features are shared between the sequences of Groups II+ and, accordingly, these groups lack unity a priori.

Groups I and II+ share the technical features including: an antibody or antigen binding fragment thereof that binds to human FLT3 and comprises a light chain sequence and a heavy chain sequence. Groups II+ share the additional technical features including: a monoclonal antibody.

However, these shared technical features are previously disclosed by US 2012/0328612 A1 to Grosse-Hovest et al. (hereinafter 'Grosse-Hovest').

Grosse-Hovest discloses an antibody or antigen binding fragment thereof that binds to human FLT3 (an antibody or antigen binding fragment thereof that binds to human FLT3; paragraph [0005]) and comprises a light chain sequence (and comprises a light chain sequence; paragraphs [0005], [0011]) and a heavy chain sequence (and a heavy chain sequence; paragraphs [0005], [0011]); a monoclonal antibody (a monoclonal antibody; paragraph [0035]).

Since none of the special technical features of the Groups I and II+ inventions is found in more than one of the inventions, and since all of the shared technical features are previously disclosed by the Grosse-Hovest reference, unity of invention is lacking.