Abstract:
Provided herein are antibodies that specifically bind to GPRC5D. Also described are related polynucleotides capable of encoding the provided GPRC5D-specific antibodies or antigen-binding fragments, cells expressing the provided antibodies or antigen-binding fragments, as well as associated vectors and detectably labeled antibodies or antigen-binding fragments. In addition, methods of using the provided antibodies are described. For example, the provided antibodies may be used to diagnose, treat, or monitor GPRC5D-expressing cancer progression, regression, or stability; to determine whether or not a patient should be treated for cancer; or to determine whether or not a subject is afflicted with GPRC5D-expressing cancer and thus may be amenable to treatment with a GPRC5D-specific anti-cancer therapeutic, such as the multispecific antibodies against GPRC5D and CD3 described herein.

Figure 1

[Continued on next page]
Declarations under Rule 4.17:
— as to applicant’s entitlement to apply for and be granted a patent (Rule 4.17(H))
— as to the applicant’s entitlement to claim the priority of the earlier application (Rule 4.17(in))

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))
— with sequence listing part of description (Rule 5.2(a))

Date of publication of the international search report:
01 March 2018 (01.03.2018)
A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/28 A61K39/395 A61P35/02
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)
C07K 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, WPI Data, BIOSIS, CHEM ABS Data, Sequence Search, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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[ ] 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
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O: document referring to an oral disclosure, use, exhibition or other means
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A: document member of the same patent family

Date of the actual completion of the international search: 5 January 2018

Date of mailing of the international search report: 02/02/2018

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:
Bernhardt, W ebke

Form PCT/ISA/210 (second sheet) (April 2005)
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<td>COHEN YOSSI ET AL: &quot;GPRC5D is a promi sing marker for monitoring the tumor load and to target multiple myeloma cells.&quot;, HEMATOLOGY (AMSTERDAM, NETHERLANDS) NOV 2013, vol. 18, no. 6, November 2013 (2013-11), pages 348-351, XP009195526, ISSN: 1607-8454, Abstract, tables 1-2</td>
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# INTERNATIONAL SEARCH REPORT

### 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. [x] 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.:

   1-6, 8, 12-29, 32, 43-65

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.

- [x] No protest accompanied the payment of additional search fees.
This International Search Authority found multiple (groups of)
inventions in this international application, as follows:

1. claims: 29 (completely); 1-6, 12-28, 43-65 (partially)

An isolated anti body, or anti gen-bi n fragment thereof,
that binds specifically to GPRC5D comprising the 6 CDRs
with Seq ID No. 1, 5, 9, 13, 16, 19 (i.e. the CDRs of anti body
designated GC5B81 according to table 1); an isolated
GPRC5D x CD3 bi specific anti body comprising said CDRs; an isolated
cell expressing said anti body or bi specific anti body; a
medical use of said bi specific anti body; a pharmaceuti
cal composition comprising said bi specific anti body; a method
for generating said bi specific anti body; an isolated
synthetic polynucleotides encoding a chain of said bi specific
anti body; a kit comprising said bi specific anti body or said
polynucleotides
d---

2-3. claims: 1-28, 30-65 (all partially)

An isolated anti body, or anti gen-biding fragment thereof,
that binds specifically to GPRC5D comprising the 6 CDRs
of anti body designated GC5B465 to GC5B599 according to
respectively; an isolated GPRC5D x CD3 bi specific anti body
comprising said CDRs; an isolated cell expressing said
anti body or bi specific anti body; a medical use of said
bi specific anti body; a pharmaceuti cal composition comprising
said bi specific anti body; a method for generating said
bi specific anti body; an isolated synthetic polynucleotides encoding a
chain of said bi specific anti body; a kit
comprising said bi specific anti body or said polynucleotides
d---

4. claims: 32 (completely); 1-5, 8, 12-28, 43-65 (partially)

An isolated anti body, or anti gen-biding fragment thereof,
that binds specifically to GPRC5D comprising the 6 CDRs
with Seq ID No. 4, 8, 12, 15, 18 and 21 (i.e. the CDRs of
anti body designated GC5B596 according to table 1),
respectively; an isolated GPRC5D x CD3 bi specific anti body
comprising said CDRs; an isolated cell expressing said
anti body or bi specific anti body; a medical use of said
bi specific anti body; a pharmaceuti cal composition comprising
said bi specific anti body; a method for generating said
bi specific anti body; an isolated synthetic polynucleotides encoding a
chain of said bi specific anti body; a kit
comprising said bi specific anti body or said polynucleotides
d---

5-13. claims: 1-28, 30-65 (all partially)

An isolated anti body, or anti gen-biding fragment thereof,
that binds specifically to GPRC5D comprising the 6 CDRs of
anti body designated GC5B382 to GC5B601 according to table 1,
respectively; an isolated GPRC5D x CD3 bispecific antibody comprising said CDRs; an isolated cell expressing said anti body or bispecific antibody; a medical use of said bispecific antibody; a pharmaceutical composition comprising said bispecific antibody; a method for generating said bispecific antibody; an isolated synthetic polynucleotide encoding a chain of said bispecific antibody; a kit comprising said bispecific antibody or said polynucleotide.
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<td>EP 1468694 A1</td>
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<td>JP WO2003055507 A1</td>
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