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Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

Published:

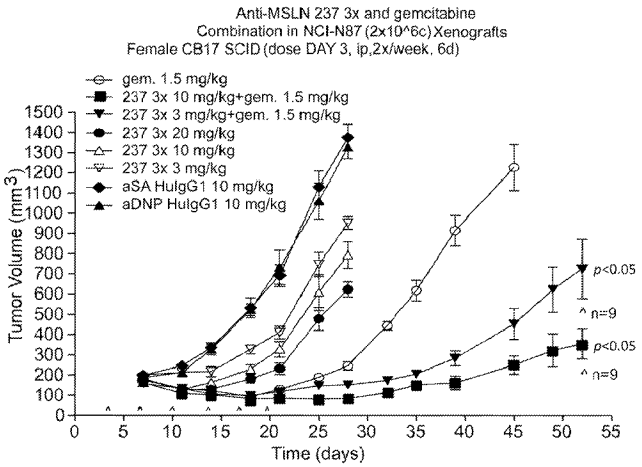
— *with international search report (Art. 21(3))*

[Continued on next page]

(54) **Title**: ANTI-MESOTHELIN BINDING PROTEINS

FIG. 17

Combining 237 3x anti Human MSLN and Gemcitabine Mediate Greater than Additive Anti-Tumor Activity in the N87 Xenograft Model



(57) **Abstract**: The present disclosure provides compositions and methods relating to antigen binding proteins, in particular, antibodies and bispecific antibodies which specifically bind to mesothelin. The disclosure provides nucleic acids encoding such antigen binding proteins and antibodies and methods of making and using such antibodies, including methods of treating and preventing cancer or other hypoproliferative disorders and related disorders by administering such antigen binding proteins and antibodies to a subject in need of such treatment.

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— *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))*

(88) Date of publication of the international search report:
13 March 2014

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2013/047674

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/30 A61K47/48
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, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2009/045957 A1 (MEDAREX INC [US]; TERRETT JONATHAN A [GB]; POGUE SARAH L [US]; TOY KRI) 9 April 2009 (2009-04-09) the whole document	1-13, 29-45
X	WO 2009/068204 A1 (BAYER SCHERING PHARMA AG [DE]; KAHNERT ANTJE [DE]; LIGHT DAVID [US]; S) 4 June 2009 (2009-06-04) the whole document	1-13, 29-45
X	WO 2010/124797 A1 (BAYER SCHERING PHARMA AG [DE]; BERHOERSTER KERSTIN [DE]; HEISLER IRING) 4 November 2010 (2010-11-04) the whole document	1-13, 29-45

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[X] Further documents are listed in the continuation of Box C.

[X] 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

"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
15 January 2014	21/01/2014

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Fellows, Edward

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Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Christoph A. Schatz: "Efficacy and candidate biomarker evaluation for the anti-mesothelin antibody drug conjugate (ADC) BAY 94-9343, mesothelin-ADC in mesothelin-positive preclinical xenograft models", Cancer Research , March 2012 (2012-03), XP002711910, Retrieved from the Internet: URL:http://cancerres.aacrjournals.org/cgi/content/short/72/8_MeetingAbstracts/2726 [retrieved on 2013-08-28] the whole document	1-13, 29-45
A	DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; March 2012 (2012-03), KELLY RONAN J ET AL: "Mesothelin-Targeted Agents in Clinical Trials and in Preclinical Development", XP002711911, Database accession no. PREV201200285110 the whole document & MOLECULAR CANCER THERAPEUTICS, vol. 11, no. 3, March 2012 (2012-03), pages 517-525, ISSN: 1535-7163, DOI: 10.1158/1535-7163.MCT-11-0454	1-13, 29-45

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/047674

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.:

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-13, 29-45(all partially)

Antibody Ab237 and related subject-matter.

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2. claims: 1-13, 29-45(all partially)

Antibody Ab1.1.2 and related subject-matter.

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3. claims: 1-13, 29-45(all partially)

Antibody Ab1.33.1 and related subject-matter.

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4. claims: 1-13, 29-45(all partially)

Antibody Ab1.33.1y and related subject-matter.

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5. claims: 1-13, 29-45(all partially)

Antibody Ab1.68.1 and related subject-matter.

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6. claims: 1-13, 29-45(all partially)

Antibody Ab1.78.1 and related subject-matter.

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7. claims: 1-13, 29-45(all partially)

Antibody Ab1.119.1 and related subject-matter.

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8. claims: 1-13, 29-45(all partially)

Antibody Ab2.69.2 and related subject-matter.

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9. claims: 1-13, 29-45(all partially)

Antibody Ab2.69.2-cv and related subject-matter.

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10. claims: 1-13, 29-45(all partially)

Antibody Ab1.58 and related subject-matter.

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11. claims: 1-13, 29-45(all partially)

Antibody Ab2.69.2-s and related subject-matter.

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12. claims: 1-13, 29-45(all partially)

Antibody Ab1.51 and related subject-matter.

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13. claims: 24-26(completely); 14-23, 27, 28, 33-45(partially)

Bispecific antibody VH(Ab237; SEQ ID Nos 45-47 and 86)-VL(Ab237; SEQ ID Nos 9-11 and 72)-VH(CD3; SEQ ID Nos115-117 and 118)-VL(CD3; SEQ ID Nos 112-114 and 120): MSLN 237-BiTE and related subject-matter.

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14. claims: 14-23, 28, 33-45(all partially)

Bispecific antibody VH(Ab1.1.2; SEQ ID No 87)-VL(Ab1.1.2; SEQ ID No 73)-VH(CD3; SEQ ID No 118)-VL(CD3; SEQ ID No 120): MSLN 1.1.2-BiTE and related subject-matter.

---

15. claims: 14-23, 28, 33-45(all partially)

Bispecific antibody VH(Ab1.33.1; SEQ ID No 88)-VL(Ab1.33.1; SEQ ID No 74)-VH(CD3; SEQ ID No 118)-VL(CD3; SEQ ID No 120): MSLN 1.33.1-BiTE and related subject-matter.

---

16. claims: 14-23, 28, 33-45(all partially)

Bispecific antibody VH(Ab21.33.1-y; SEQ ID No 88)-VL(Ab1.33.1-y; SEQ ID No 75)-VH(CD3; SEQ ID No 118)-VL(CD3; SEQ ID No 120): MSLN 1.33.1-y-BiTE and related subject-matter.

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17. claims: 14-20, 28, 33-45(all partially)

Bispecific antibody VH(Ab1.68.1; SEQ ID No 89)-VL(Ab1.68.1; SEQ ID No 76)-VH(CD3; SEQ ID No 118)-VL(CD3; SEQ ID No 120): MSLN 1.68.1-BiTE and related subject-matter.

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18. claims: 14-20, 33-45(all partially)

Bispecific antibody VH(Ab1.78.1; SEQ ID No 90)-VL(Ab1.78.1; SEQ ID No 77)-VH(CD3; SEQ ID No 118)-VL(CD3; SEQ ID No 120): MSLN 1.78.1-BiTE and related subject-matter.

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19. claims: 14-20, 28, 33-45(all partially)

Bispecific antibody VH(Ab1.119.1; SEQ ID No

91)-VL(Ab1.119.1; SEQ ID No 78)-VH(CD3; SEQ ID No 118)-VL(CD3; SEQ ID No 120): MSLN 1.119.1-BiTE and related subject-matter.

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20. claims: 14-20, 28, 33-45(all partially)

Bispecific antibody VH(Ab2.69.2; SEQ ID No 92)-VL(Ab2.69.2; SEQ ID No 79)-VH(CD3; SEQ ID No 118)-VL(CD3; SEQ ID No 120): MSLN 2.69.2-BiTE and related subject-matter.

---

21. claims: 14-20, 33-45(all partially)

Bispecific antibody VH(Ab2.69.2-s; SEQ ID No 92)-VL(Ab2.69.2-s; SEQ ID No 80)-VH(CD3; SEQ ID No 118)-VL(CD3; SEQ ID No 120): MSLN 2.69.2-s-BiTE and related subject-matter.

---

22. claims: 14-20, 33-45(all partially)

Bispecific antibody VH(Ab2.69.2-cv; SEQ ID No 92)-VL(Ab2.69.2-cv; SEQ ID No 81)-VH(CD3; SEQ ID No 118)-VL(CD3; SEQ ID No 120): MSLN 2.69.2-cv-BiTE and related subject-matter.

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23. claims: 14-23, 28, 33-45(all partially)

Bispecific antibody VH(Ab1.58; SEQ ID No 93)-VL(Ab1.58; SEQ ID No 82)-VH(CD3; SEQ ID No 118)-VL(CD3; SEQ ID No 120): MSLN 1.58-BiTE and related subject-matter.

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24. claims: 14-23, 28, 33-45(all partially)

Bispecific antibody VH(Ab1.51; SEQ ID No 94)-VL(Ab1.51; SEQ ID No 83)-VH(CD3; SEQ ID No 118)-VL(CD3; SEQ ID No 120): MSLN 1.51-BiTE and related subject-matter.

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25. claims: 14-23, 27, 28, 33-45(all partially)

Bispecific antibody VLAb237-VHAb237-VHCD3-VLCD3 (SEQ ID No. 129) and related subject-matter.

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26. claims: 14-23, 28, 33-45(all partially)

Bispecific antibody VLAb1.58-VHAb1.58-VHCD3-VLCD3 (SEQ ID Nos. 159 and 122 respectively) and related subject-matter.

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27. claims: 14-23, 28, 33-45(all partially)

Bispecific antibody VLAb1.33.1-y-VHAb1.33.1-y-VHCD3-VLCD3 (SEQ ID Nos. 163 and 122 respectively) and related subject-matter.

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28. claims: 14-23, 28, 33-45(all partially)

Bispecific antibody VLAb1.51-VHAb1.51-VHCD3-VLCD3 (SEQ ID Nos. 165 and 122 respectively) and related subject-matter.

---

29. claims: 14-23, 28, 33-45(all partially)

Bispecific antibody VLAb1.119.1-VHAb1.119.1-VHCD3-VLCD3 (SEQ ID Nos. 169 and 122 respectively) and related subject-matter.

---

30. claims: 14-20, 33-45(all partially)

Bispecific antibody VLAb1.68.1-VHAb1.68.1-VHCD3-VLCD3 (SEQ ID Nos. 171 and 122 respectively) and related subject-matter.

---

31. claims: 14-20, 33-45(all partially)

Bispecific antibody VLAb2.69.2-VHAb12.69.2-VHCD3-VLCD3 (SEQ ID Nos. 173 and 122 respectively) and related subject-matter.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2013/047674

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