

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference P0177-WO-PCT	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/EP2022/077817	International filing date (<i>day/month/year</i>) 6 October 2022 (06-10-2022)	(Earliest) Priority Date (<i>day/month/year</i>) 8 October 2021 (08-10-2021)
Applicant GENMAB A/S		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 10 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of:

- ☒ the international application in the language in which it was filed
☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6bis(a)).

c. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II)

3. ☒ **Unity of invention is lacking** (see Box No III)

4. With regard to the **title**,

- ☒ the text is approved as submitted by the applicant
☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- ☒ the text is approved as submitted by the applicant
☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. _____
☐ as suggested by the applicant
☐ as selected by this Authority, because the applicant failed to suggest a figure
☐ as selected by this Authority, because this figure better characterizes the invention
- b. ☒ none of the figures is to be published with the abstract

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP2022/077817

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:
 - a. ☒ forming part of the international application as filed.
 - b. ☐ furnished subsequent to the international filing date for the purposes of international search (Rule 13*ter*.1(a)).

☐ accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.
2. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this report has been established to the extent that a meaningful search could be carried out without a WIPO Standard ST.26 compliant sequence listing.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2022/077817

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.:
1-48, 58-60

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/EP2022/077817

A. CLASSIFICATION OF SUBJECT MATTER INV. C07K16/28 A61K39/395 A61P35/00 A61K39/00 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) A61K A61P C07K		
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, FSTA, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2008/119567 A2 (MICROMET AG [DE]; EBERT EVELYN [DE] ET AL.) 9 October 2008 (2008-10-09) cited in the application See e.g. SEQ ID NOs: 1113 and 1118; Example 29 from pages 176-183; Figures 46 and 47 -----	1-48, 58-60
Y	US 2019/284278 A1 (RADEMAKER RIK [NL] ET AL) 19 September 2019 (2019-09-19) See e.g. SEQ ID NOs: 1, 2, 3, 6, 7, 176; paragraphs 846-855, 859, 861, 715 and 716; Table 1 VL CDR2; claim 29(e) ----- --/--	1-48, 58-60
☒ 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		Date of mailing of the international search report
30 November 2022		30/01/2023
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 Valcárcel, Rafael

International application No
PCT/EP2022/077817

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

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2022/077817

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2014/006217 A1 (GENMAB BV [NL]) 9 January 2014 (2014-01-09) See e.g. page 43, lines 7 and 8; page 43, 7th paragraph -----	1-48, 58-60
Y	US 2021/009718 A1 (AMBROGELLY ALEXANDRE [US] ET AL) 14 January 2021 (2021-01-14) See e.g. paragraph 106 -----	1-48, 58-60
Y	WO 2019/025545 A1 (GENMAB AS [DK]; BIONTECH AG [DE]) 7 February 2019 (2019-02-07) See e.g. Example 13 -----	1-48, 58-60
Y	CHRISTIAN KLEIN ET AL: "Progress in overcoming the chain association issue in bispecific heterodimeric IgG antibodies", MABS, vol. 4, no. 6, 1 November 2012 (2012-11-01), pages 653-663, XP055106060, ISSN: 1942-0862, DOI: 10.4161/mabs.21379 See e.g. Figures 2 and 5 -----	1-48, 58-60
Y	DENNIS R. GOULET ET AL: "Kinetic mechanism of controlled Fab-arm exchange for the formation of bispecific immunoglobulin G1 antibodies", JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 293, no. 2, 17 November 2017 (2017-11-17), pages 651-661, XP055549625, US ISSN: 0021-9258, DOI: 10.1074/jbc.RA117.000303 See e.g. the abstract -----	1-48, 58-60

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2022/077817

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2008119567 A2	09-10-2008	CN 101687915 A	31-03-2010
		CN 103694350 A	02-04-2014
		CY 1120822 T1	11-12-2019
		DK 2520590 T3	12-11-2018
		EP 2155783 A2	24-02-2010
		EP 2520590 A2	07-11-2012
		EP 3461842 A1	03-04-2019
		ES 2432792 T3	05-12-2013
		ES 2695047 T3	28-12-2018
		FI 2155783 T4	15-12-2022
		HR P20181902 T1	11-01-2019
		IL 201340 A	30-11-2015
		JP 2010524851 A	22-07-2010
		KR 20150140399 A	15-12-2015
		KR 20170102032 A	06-09-2017
		LT 2520590 T	10-09-2018
		NZ 580755 A	25-05-2012
		PL 2155783 T3	31-01-2014
		PL 2520590 T3	28-02-2019
		PT 2155783 E	07-11-2013
		RS 53008 B	30-04-2014
		RU 2009136912 A	10-05-2011
		SG 182234 A1	30-07-2012
		SG 195609 A1	30-12-2013
		SG 10201808730V A	29-11-2018
		SI 2155783 T1	30-10-2013
		SI 2520590 T1	31-12-2018
		WO 2008119567 A2	09-10-2008
		ZA 200907117 B	30-03-2011
US 2019284278 A1	19-09-2019	AU 2016293073 A1	01-02-2018
		BR 112018000696 A2	18-09-2018
		CA 2992380 A1	19-01-2017
		CN 108368172 A	03-08-2018
		CN 114989302 A	02-09-2022
		EA 201890305 A1	31-07-2018
		EP 3322727 A1	23-05-2018
		IL 256562 A	28-02-2018
		JP 2018526981 A	20-09-2018
		JP 2022023862 A	08-02-2022
		KR 20180030635 A	23-03-2018
		US 2019284278 A1	19-09-2019
		US 2022380464 A1	01-12-2022
		US 2022389101 A1	08-12-2022
		WO 2017009442 A1	19-01-2017
US 2020239579 A1	30-07-2020	AU 2018231618 A1	03-10-2019
		BR 112019018533 A2	14-04-2020
		CA 3055127 A1	13-09-2018
		CN 110573524 A	13-12-2019
		EP 3592769 A1	15-01-2020
		IL 269002 A	31-10-2019
		JP 2020511133 A	16-04-2020
		KR 20190128667 A	18-11-2019
		MA 49823 A	21-04-2021
		SG 11201908088R A	30-10-2019
		US 2020239579 A1	30-07-2020
		WO 2018162749 A1	13-09-2018

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2022/077817

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2020068774	A1	02-04-2020	AU 2019349662 A1 29-04-2021
		CA 3155293 A1 02-04-2020	
		EP 3856778 A1 04-08-2021	
		US 2020095330 A1 26-03-2020	
		WO 2020068774 A1 02-04-2020	
US 2017073421	A1	16-03-2017	AU 2012266487 A1 21-11-2013
		BR 112013031198 A2 29-11-2016	
		CA 2838497 A1 13-12-2012	
		CN 103596982 A 19-02-2014	
		DK 2718322 T3 03-12-2018	
		DK 3424953 T3 02-11-2020	
		DK 3798230 T3 31-10-2022	
		EP 2718322 A1 16-04-2014	
		EP 3424953 A1 09-01-2019	
		EP 3798230 A1 31-03-2021	
		ES 2693647 T3 13-12-2018	
		ES 2929575 T3 30-11-2022	
		IL 229254 A 28-09-2017	
		JP 6141834 B2 07-06-2017	
		JP 6416177 B2 31-10-2018	
		JP 2014523408 A 11-09-2014	
		JP 2017081941 A 18-05-2017	
		KR 20140036261 A 25-03-2014	
		PL 2718322 T3 31-07-2019	
		PL 3424953 T3 25-01-2021	
		PT 3424953 T 03-11-2020	
		RU 2013155029 A 20-07-2015	
		TW 201311724 A 16-03-2013	
		US 2013004514 A1 03-01-2013	
		US 2013295116 A1 07-11-2013	
		US 2015044231 A1 12-02-2015	
		US 2017073421 A1 16-03-2017	
		US 2020017599 A1 16-01-2020	
		US 2021238300 A1 05-08-2021	
		WO 2012168199 A1 13-12-2012	
US 2021163594	A1	03-06-2021	EP 3781204 A1 24-02-2021
			US 2021163594 A1 03-06-2021
			WO 2019204522 A1 24-10-2019
WO 2006105062	A2	05-10-2006	US 2010104564 A1 29-04-2010
			US 2011123440 A1 26-05-2011
			WO 2006104989 A2 05-10-2006
			WO 2006105062 A2 05-10-2006
WO 2014006217	A1	09-01-2014	AU 2013285355 A1 29-01-2015
			AU 2018203510 A1 07-06-2018
			AU 2020202410 A1 30-04-2020
			AU 2022259785 A1 01-12-2022
			BR 112015000167 A2 08-08-2017
			CN 104736174 A 24-06-2015
			EP 2869845 A1 13-05-2015
			EP 2943507 A1 18-11-2015
			EP 3738979 A1 18-11-2020
			JP 6514103 B2 15-05-2019
			JP 6604851 B2 13-11-2019

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2022/077817

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		JP 2015524387 A	24-08-2015
		JP 2016508153 A	17-03-2016
		JP 2022115955 A	09-08-2022
		PL 2943507 T3	27-07-2020
		SG 10201605703T A	29-09-2016
		SG 11201408646V A	29-01-2015
		SI 2943507 T1	31-07-2020
		US 2015175707 A1	25-06-2015
		US 2015337049 A1	26-11-2015
		US 2020332022 A1	22-10-2020
		WO 2014006217 A1	09-01-2014
		WO 2014108483 A1	17-07-2014
US 2021009718 A1	14-01-2021	AR 119235 A1	01-12-2021
		AU 2020301161 A1	06-01-2022
		BR 112021026376 A2	10-05-2022
		CA 3142513 A1	30-12-2020
		CL 2021003457 A1	07-10-2022
		CN 114245807 A	25-03-2022
		CO 2021017741 A2	17-01-2022
		CR 20210687 A	03-03-2022
		EP 3990476 A1	04-05-2022
		IL 288373 A	01-01-2022
		JP 2022539528 A	12-09-2022
		KR 20220032568 A	15-03-2022
		PE 20220231 A1	07-02-2022
		TW 202115128 A	16-04-2021
		US 2021009718 A1	14-01-2021
		US 2021070887 A1	11-03-2021
		US 2022049021 A1	17-02-2022
		WO 2020263830 A1	30-12-2020
WO 2019025545 A1	07-02-2019	AU 2018309339 A1	20-02-2020
		BR 112020001944 A2	04-08-2020
		CA 3071211 A1	07-02-2019
		CN 111406067 A	10-07-2020
		EP 3661960 A1	10-06-2020
		IL 272159 A	31-03-2020
		JP 2020529438 A	08-10-2020
		KR 20200064062 A	05-06-2020
		MA 49753 A	10-06-2020
		SG 11202000198Q A	27-02-2020
		US 2020165349 A1	28-05-2020
		US 2021163616 A1	03-06-2021
		US 2021269541 A1	02-09-2021
		US 2021277133 A1	09-09-2021
		WO 2019025545 A1	07-02-2019

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-48, 58-60

A multispecific antibody as defined in claim 1. A nucleic acid construct or a combination of nucleic acid constructs encoding said multispecific antibody. Expression vector, delivery vehicle, recombinant host cell, composition as defined in claims 28-36. The multispecific antibody for the uses as defined in claims 37-43. The above products that have been administered as defined in claim 44. Methods for producing the multispecific antibody as defined in claims 45, 46, 58 and 59. Kits and diagnostic compositions as defined in claims 47 and 48. A multispecific antibody obtained by the method as described in claims 58 or 59.

2. claims: 49-51

An antibody as defined in claim 49.

3. claims: 52-57

An antibody as defined in claim 52.
