

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 118003-10520		FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2020/040642	International filing date (day/month/year) 02 July 2020	(Earliest) Priority Date (day/month/year) 03 July 2019	
Applicant REGENERON PHARMACEUTICALS, INC.			

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 6 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. 1A
☐ 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.

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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:

☒ in the form of an Annex C/ST.25 text file.

☐ on paper or in the form of an image file.

b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

c. ☐ furnished subsequent to the international filing date for the purposes of international search only:

☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

SEQ ID NOs: 2, 10, 22, 30, 42, 50, 62, 70, 82, 90, 102, 110, 112, 122, 130, 142, 150, 162, 170, 180, 186, 195, 196, 203, 211, 219, 230, 238, 250, 258, 269, 271, 273, 274, 276, 277, 280, and 291 were searched.

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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.: 16-57, 62-75
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:

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.:

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.

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Box No. IV Text of the abstract (Continuation of item 5 of the first sheet)

The present disclosure provides antigen-binding proteins that specifically bind to an HLA-displayed New York esophageal squamous cell carcinoma 1 (NY-ESO-1) peptide, and therapeutic and diagnostic methods of using those binding proteins. The antigen-binding proteins of the present disclosure bind with a high degree of specificity to HLA-displayed NY-ESO-1 and do not bind to HLA-displayed peptides that differ by 2, 3, 4, 5 or more amino acids.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 38/00; A61K 39/00; A61K 39/395; C07K 7/06; C07K 16/18; C12N 15/13 (2020.01)

CPC - A61K 38/00; A61K 39/00; A61K 2039/505; C07K 7/06; C07K 14/47; C07K 16/00; C07K 2317/56; C07K 2319/00 (2020.08)

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	IRVING et al. "Interplay between T cell receptor binding kinetics and the level of cognate peptide presented by major histocompatibility complexes governs CD8+ T cell responsiveness," J Biol Chem, 01 May 2012 (01.05.2012), Vol. 87, Pgs. 23068-23078. entire document	1-7
A	US 2018/0371049 A1 (ADAPTIMMUE LIMITED) 27 December 2018 (27.12.2018) entire document	1-15, 58-61
A	DHANIK et al. "In-silico discovery of cancer-specific peptide-HLA complexes for targeted therapy," BMC Bioinformatics, 20 July 2016 (20.07.2016), Vol.17, 286, Pgs. 1-14. entire document	1-15, 58-61
A	DUNBAR et al. "Examining Variable Domain Orientations in Antigen Receptors Gives Insight into TCR-Like Antibody Design," PLoS Comput Biol, 18 September 2014 (18.09.2014), Vol. 10, e1003852, Pgs. 1-10. entire document	1-15, 58-61
A	US 2019/0002522 A1 (HEALTH RESEARCH, INC.) 03 January 2019 (03.01.2019) entire document	1-15, 58-61
A	US 2003/0175250 A1 (JAGER et al) 18 September 2003 (18.09.2003) entire document	1-15, 58-61
A	MAUS et al. "An MHC-restricted antibody-based chimeric antigen receptor requires TCR-like affinity to maintain antigen specificity," Mol Ther Oncolytics, 11 January 2017 (11.01.2017), Vol. 3, Pgs. 1-9. entire document	1-15, 58-61

☒ 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

13 October 2020

Date of mailing of the international search report

22 OCT 2020

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents

P.O. Box 1450, Alexandria, VA 22313-1450

Facsimile No. 571-273-8300

Authorized officer

Blaine R. Copenheaver

Telephone No. PCT Helpdesk: 571-272-4300

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2018/0258187 A1 (MEMORIAL SLOAN KETTERING CANCER CENTER et al) 13 September 2018 (13.09.2018) entire document	1-15, 58-61
A	US 2016/0081314 A1 (REGENERON PHARMACEUTICALS, INC.) 24 March 2016 (24.03.2016) entire document	1-15, 58-61
A	STEWART-JONES et al. "Rational development of high-affinity T-cell receptor-like antibodies," Proc Natl Acad Sci USA, 23 March 2009 (23.03.2009), Vol. 106, Pgs. 5784-5788. entire document	1-15, 58-61
A	ZOETE et al. "Structure-Based, Rational Design of T Cell Receptors," Front Immunol, 12 September 2013 (12.09.2013), Vol. 4, 268, Pgs. 1-19. entire document	1-15, 58-61