

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference B3168PC00	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/EP2020/086600	International filing date (<i>day/month/year</i>) 17 December 2020 (17-12-2020)	(Earliest) Priority Date (<i>day/month/year</i>) 17 December 2019 (17-12-2019)
Applicant OSE IMMUNOTHERAPEUTICS		

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 8 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 43.6**bis**(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

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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:

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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.:
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.:

2, 3(completely); 1, 5-24(partially)

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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International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K14/54 A61K38/00
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)
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, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2006/061219 A2 (MERCK PATENT GMBH [DE]; GILLIES STEPHEN D [US]; WAY JEFFREY C [US]) 15 June 2006 (2006-06-15) cited in the application abstract; claims 1,9,19 -----	1-3,5-24
Y	WO 2005/063820 A2 (MERCK PATENT GMBH [DE]; LAUDER SCOTT [US]; GILLIES STEPHEN D [US]) 14 July 2005 (2005-07-14) cited in the application claims 1,7 -----	1-3,5-24
A	WO 2008/003473 A2 (MERCK PATENT GMBH [DE]; GILLIES STEPHEN D [US]) 10 January 2008 (2008-01-10) claim 1; example 3 ----- -/-	1-3,5-24



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

22 March 2021

Date of mailing of the international search report

07/06/2021

Name and mailing address of the ISA/

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Authorized officer

Griesinger, Irina

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	COSENZA L ET AL: "Disulfide bond assignment in human interleukin-7 by matrix-assisted laser desorption/ionization mass spectroscopy and site-directed cysteine to serine mutational analysis", JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY, US, vol. 272, no. 52, 26 December 1997 (1997-12-26), pages 32995-33000, XP002226701, ISSN: 0021-9258, DOI: 10.1074/JBC.272.52.32995 abstract	1-3,5-24
A	----- THOMAS LIST ET AL: "Immunocytokines: a review of molecules in clinical development for cancer therapy", CLINICAL PHARMACOLOGY: ADVANCES AND APPLICATIONS, 1 August 2013 (2013-08-01), page 29, XP055289369, DOI: 10.2147/CPAA.S49231 abstract	1-3,5-24
A	----- STROHL ET AL: "Optimization of Fc-mediated effector functions of monoclonal antibodies", CURRENT OPINION IN BIOTECHNOLOGY, LONDON, GB, vol. 20, no. 6, 1 December 2009 (2009-12-01), pages 685-691, XP026778879, ISSN: 0958-1669, DOI: 10.1016/J.COPBIO.2009.10.011 [retrieved on 2009-11-04] tables 2,3	1-3,5-24
Y	----- LARRY COSENZA ET AL: "Comparative model building of interleukin-7 using interleukin-4 as a template: A structural hypothesis that displays atypical surface chemistry in helix D important for receptor activation", PROTEIN SCIENCE, vol. 9, no. 5, 1 January 2000 (2000-01-01), pages 916-926, XP055539734, US ISSN: 0961-8368, DOI: 10.1110/ps.9.5.916 abstract	1-3,5-24

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2020/086600

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2006061219	A2	15-06-2006	AT 465176 T 15-05-2010
		AU 2005313492 A1 15-06-2006	
		BR PI0519000 A2 23-12-2008	
		CA 2591297 A1 15-06-2006	
		CN 101072793 A 14-11-2007	
		EP 1819728 A2 22-08-2007	
		ES 2342964 T3 20-07-2010	
		JP 4937132 B2 23-05-2012	
		JP 2008522600 A 03-07-2008	
		KR 20070085886 A 27-08-2007	
		US 2006141581 A1 29-06-2006	
		WO 2006061219 A2 15-06-2006	
		ZA 200705559 B 29-10-2008	
WO 2005063820	A2	14-07-2005	AT 393169 T 15-05-2008
		AU 2004309050 A1 14-07-2005	
		BR PI0418286 A 02-05-2007	
		CA 2551915 A1 14-07-2005	
		CN 1898262 A 17-01-2007	
		DE 602004013372 T2 02-07-2009	
		DK 1699822 T3 04-08-2008	
		EP 1699822 A2 13-09-2006	
		ES 2305886 T3 01-11-2008	
		JP 2008502317 A 31-01-2008	
		KR 20060112673 A 01-11-2006	
		PL 1699822 T3 29-08-2008	
		PT 1699822 E 30-07-2008	
		RU 2369616 C2 10-10-2009	
		US 2005164352 A1 28-07-2005	
		US 2009010875 A1 08-01-2009	
		US 2011243887 A1 06-10-2011	
		WO 2005063820 A2 14-07-2005	
WO 2008003473	A2	10-01-2008	AU 2007271398 A1 10-01-2008
		CA 2656700 A1 10-01-2008	
		EP 2038417 A2 25-03-2009	
		IL 196282 A 30-05-2013	
		JP 2009542592 A 03-12-2009	
		JP 2013100297 A 23-05-2013	
		US 2008025947 A1 31-01-2008	
		US 2013017168 A1 17-01-2013	
		WO 2008003473 A2 10-01-2008	

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 2, 3(completely); 1, 5-24(partially)

relate to a fusion protein comprising an IL-7 variant and a binding moiety, wherein the IL-7 variant has reduced affinity for the IL-7 receptor and an improved pharmacogenetic property; the corresponding nucleic acids, host cells, compositions and uses.

1.1. claims: 2(completely); 1, 5-24(partially)

relate to a fusion protein comprising an IL-7 variant and a binding moiety, wherein the IL-7 variant has reduced affinity for the IL-7 receptor and an improved pharmacogenetic property said variant being characterized by the substitution W142H/F/Y; the corresponding nucleic acids, host cells, compositions and uses.

1.2. claims: 3(completely); 1, 5-24(partially)

relate to a fusion protein comprising an IL-7 variant and a binding moiety, wherein the IL-7 variant has reduced affinity for the IL-7 receptor and an improved pharmacogenetic property said variant being characterized by the substitution of four cysteine residues by serine residues; the corresponding nucleic acids, host cells, compositions and uses.

2. claims: 4(completely); 1, 5-24(partially)

relate to a fusion protein comprising an IL-7 variant and a binding moiety, wherein the IL-7 variant has reduced affinity for the IL-7 receptor and an improved pharmacogenetic property said variant being characterized by the substitution D74E/Q/N; the corresponding nucleic acids, host cells, compositions and uses.

3. claims: 1, 5-24(all partially)

relate to a fusion protein comprising an IL-7 variant and a binding moiety, wherein the IL-7 variant has reduced affinity for the IL-7 receptor and an improved pharmacogenetic property said variant being characterized by the substitution Q11E; the corresponding nucleic acids, host cells, compositions and uses.

4. claims: 1, 5-24(all partially)

relate to a fusion protein comprising an IL-7 variant and a binding moiety, wherein the IL-7 variant has reduced

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

affinity for the IL-7 receptor and an improved pharmacogenetic property said variant being characterized by the substitution Y12F; the corresponding nucleic acids, host cells, compositions and uses.

5. claims: 1, 5-24(all partially)

relate to a fusion protein comprising an IL-7 variant and a binding moiety, wherein the IL-7 variant has reduced affinity for the IL-7 receptor and an improved pharmacogenetic property said variant being characterized by the substitution M17L; the corresponding nucleic acids, host cells, compositions and uses.

6. claims: 1, 5-24(all partially)

relate to a fusion protein comprising an IL-7 variant and a binding moiety, wherein the IL-7 variant has reduced affinity for the IL-7 receptor and an improved pharmacogenetic property said variant being characterized by the substitution Q22E; the corresponding nucleic acids, host cells, compositions and uses.

7. claims: 1, 5-24(all partially)

relate to a fusion protein comprising an IL-7 variant and a binding moiety, wherein the IL-7 variant has reduced affinity for the IL-7 receptor and an improved pharmacogenetic property said variant being characterized by the substitution K81R; the corresponding nucleic acids, host cells, compositions and uses.
